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THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY

Vol. XVI. APRIL, 1936 No. 64

Original Papers

MULTIPLE METASTATIC TUMOURS IN THE BRAIN ARISING FROM PRIMARY BRONCHIAL CARCINOMA *

By

W. E. CARNEGIE DICKSON AND C. WORSTER-DROUGHT, LONDON

THE clinical and pathological investigation of multiple metastatic tumours of the brain arising from primary bronchial carcinomas is full of snares and pitfalls for the neurological physician, surgeon and pathologist; and, although bronchogenic carcinoma with secondary growths in the brain produces a now fairly well recognized and not uncommon syndrome, its diagnosis is still sometimes made only in the post-mortem room; and even there difficulties may occasionally arise in its recognition.

Ten years ago, in a text-book [1] for which one of us, together with Professor J. M. Beattie, was responsible, the statement was made that 'Primary tumours of the lung are extremely rare. Osteomas, chondromas, and sarcomas occur, but the most usual primary tumours are columnar-celled cancers—originating, probably, from some part of the bronchi or from the mucous glands'; while under the heading 'Tumours of the Brain' we merely stated that 'Secondary cancer is also rare.' Similarly, Ewing, in the third edition (1928) of his book, *Neoplastic Diseases*, p. 851, gives the frequency of primary malignant tumours of the lung at about 1 per cent. of all cancers, his statistics being taken from between 16,000 and 17,000 autopsies on cancer cases.

These statements now require modification, as both in our own experience and in that of others, the frequency of bronchial carcinomas—whether they are described as such or as 'Oat-celled Sarcoma of the Mediastinum' [2] [3]: as 'Tumours of the Mediastinum and Lung' [4]: as 'Primary Lung Tumours,' [5]

* Communicated at Meetings of the Neurological Section of the Royal Society of Medicine, London, May 17, 1934, and February 21, 1935. From the West End Hospital for Diseases of the Nervous System, London.

or as 'Primary Carcinoma of the Lung' [6]—has increased remarkably during the last ten years, not only in this country but on the continent of Europe and in America and elsewhere. Recent writers give figures up to 15 per cent. or more, and Percival Bailey,[7] writing in America, gives this increasing frequency of carcinoma of the lung as 7 to 10 per cent. of all carcinomas, and the age incidence as especially between 40 and 60. The marked tendency for such bronchogenic carcinomas to produce metastases in the brain is indicated by figures such as 37, 41, and 47 per cent. in various recorded series of such cases.

Papers dealing with the histological aspect of the subject have, as is natural, been written mainly from the point of view of those interested in the lung condition rather than in its neurological aspects. Practically all recent writers dealing with the pathology of these tumours are agreed that they are of the nature of carcinomas arising from the bronchial mucous membrane. Shennan [4] of Aberdeen gives an excellent description of the naked-eye and histological appearances of such intrathoracic tumours but in the main portion of his paper makes no special reference to the frequency of cerebral metastases. In an appendix, however, in giving the details of some of his 31 cases, he mentions one (Case 16) in which there were such secondary nodules in the brain, the tumour being histologically a columnar-celled papilloma, occurring in a male aged 62. Dr. Norah Schuster in her paper on the 'Ætiology and Pathology of Primary Lung Tumours' [5] gives details of 62 such cases, and draws attention to the occurrence of metastases in the brain in which, she states, 'they are nearly all small-cell tumours,' previously often mistaken for, or designated as, 'sarcomas.' She also points out that histologically these metastatic tumours not infrequently show varied appearances in different parts—a finding with which our own experience fully agrees. Dr. Schuster makes the valuable suggestion that, as the cells of bronchial tumours may secrete mucin, the investigation of such cases should include the use of some specific stain for that substance, such as Mayer's mucicarmine, a suggestion which we have found extremely useful.

From a statistical point of view, the paper on 'Primary Carcinoma of the Lung' by S. Levy Simpson [6] gives much valuable information. In his analysis of 139 cases occurring at the London Hospital, 19 are recorded as having metastases in the brain. This writer also calls attention to the frequency with which the clinical diagnosis has been missed; of 66 erroneously diagnosed cases, found at post-mortem to be carcinoma of the lung, there was what he terms a 'cerebral group' of 13, of which seven had been diagnosed clinically as primary cerebral tumour. For the clinical diagnosis of such cases Simpson calls attention to the significance of general wasting, dyspnœa, bronchitis, hæmoptysis, hoarseness, offensive breath (bronchiectasis) and leucocytosis. As regards latency of symptoms, some of the other records are also striking. Sehert,[8] in a series of 204 cases of tumour of the lung, found that only six had been diagnosed during life, and Wells [9] in 11 cases found only one diagnosed.

During the past two years we have had, at the West End Hospital for Diseases of the Nervous System, seven patients who on post-mortem examination were found to have died from multiple metastatic tumours of the brain arising from primary bronchial carcinomas. For purposes of comparison, Dr. Norah Schuster has kindly placed at our disposal five of her cases occurring at the Royal Chest Hospital, City Road, and our colleague, Dr. McMenemey, has provided us with two similar cases from another hospital.

Perhaps the most notable feature of the majority of these cases has been the extreme latency of the lung symptoms. In our seven West End Hospital cases, a point of interest was that all occurred in middle-aged to elderly males (with ages of 43, 45, 47, 55, 56, 61, and 64 years). McMenemey's cases were also both males, while Schuster's five cases were all females (with ages of 29, 33, 41, 42 and (?)). Both series occurred in mixed hospitals, showing that one should not make any broad generalizations with regard to age, sex, etc., from a small series of cases. It is possible, however, that in the female cases, which occurred mostly in earlier middle-age, the symptoms of the lung condition were sufficiently pronounced to cause patients to seek advice and treatment at a chest hospital; whilst in the male cases, the lung condition tended to remain more or less latent or was believed to be merely some degree of 'chronic bronchitis,' and was often completely masked by the symptoms produced by the cerebral metastases, thus causing the patients to be sent to a hospital for nervous diseases.

In the first two cases of the latter series occurring in males which we investigated, the histological appearances of the cerebral metastatic tumours were pronouncedly *papillomatous* in character, and, moreover, some of the tumours occurred actually in, or in continuity with, the choroid plexuses of the lateral ventricles. On perusing the literature of similar cases, we found several apparently identical examples of such tumours described as 'multiple malignant papillomatous tumours of the choroid plexus'; but, judging by the findings in some of our post-mortem examinations and granted that other less likely sources can be excluded, we are inclined to suspect that not a few of these have in reality been cases of multiple metastatic growths secondary to some perhaps quite inconspicuous and undetected primary bronchial carcinoma, such as is illustrated in our second case. Quite a number of cases recorded by surgical writers, especially in America, and described as 'malignant tumours of the choroid plexus' may equally well have been cerebral metastases from bronchial carcinomas. Walter E. Dandy,[10] in his recently published book entitled *Benign Encapsulated Tumors in the Lateral Ventricles of the Brain*, and, in the chapter dealing with 'Invasive and Malignant Tumors of the Lateral Ventricles,' makes the following statement, with which we fully agree:

> 'Microscopic diagnosis in the seas in other tumours attains increasing value only after correlation with the gross observations and especially with the ultimate results following extirpation. Neither the gross nor microscopic appearance of the tumour

> is as yet an infallible guide concerning the character of the tumour and at times both together fail in the task, the life history of the growth being the final test.'

The two cases of malignant tumour which Dandy records as arising from the choroid plexus *early in life* we believe to be in all probability accurately thus diagnosed ; but, from our recent experience of cases such as he describes in older patients, we have grave doubt as to the accuracy of the statement (p. 31) that the case recorded by Le Blanc (1866) was ' an unquestioned malignant tumour of the choroid plexus ' ; and we are equally uncertain about the accuracy of the diagnosis in the other cases of middle-aged to elderly patients reported by many of the older writers such as Spät [11] (1882), Bielchowsky and Unger [12] (1906, in a female aged 43, with multiple tumours both in cerebrum and cerebellum), and others. In fact we regard the diagnosis of primary malignant tumour of the choroid plexus as distinctly open to question, and we venture to suggest that in particular the history of Atlee's case [13] (1907), which Dandy quotes in some detail (p. 31), is almost pathognomonic of multiple secondary bronchogenic carcinomatous nodules in the brain. Dandy's account of this case is as follows :

> ' Atlee of Lancaster, Pennsylvania, removed a seemingly encapsulated tumour from the right Rolandic area. A splendid temporary result followed its enucleation, for the patient, who was a physician, regained his motor and sensory functions. Histological examination revealed the characteristic duplication of the choroid plexus. Doubtless the tumour was a metastatic nodule because it was cortical and not intraventricular. Another interesting feature that especially engaged the attention of Dr. Mills, who reported the case with Atlee, was paralysis of the vocal cord on the contralateral side. Dr. Mills collected many reports from the literature to prove that the paralysis was of central and not peripheral origin. We now know from extirpation of a cerebral hemisphere that paralysis of the vocal cord does not follow. Recently Dr. Atlee advised me that his patient died several months after operation from symptoms that were referred to the thorax. It was his belief that the patient died as the result of metastases from the original cerebral tumour—probably an adenocarcinoma of the choroid plexus.'

That the intrathoracic condition was the primary one and that the (presumably) multiple cerebral tumours were secondary to a bronchial carcinoma we regard as more than probable—in fact almost a certainty. Involvement of the left recurrent laryngeal nerve by mediastinal spread of the lung tumour probably accounted for the laryngeal paralysis described as occurring in the case. Temporary improvement from the relief of pressure may well have occurred after the incomplete removal of the easily enucleable tumour mass, but the inevitable regrowth from the shell of infiltrating malignant cells that remained lining the operation cavity occurred later with a fatal result. In these cases, such cerebral metastatic tumours are almost invariably multiple and the presence of the primary growth in the lung, as well as secondary metastases in the lungs themselves and in other organs, may also contribute to a rapidly fatal issue. In 1933, Hall and Fentress [14] described very fully a case which they considered to be one of ' Papilloma

Choroideum with Diffuse Central Nervous System Metastases,' any or all of the illustrations and descriptions of which might quite well have been taken from one or other of our own series of bronchogenic cases; and we suggest that, in the sections of the metastases in the central nervous system of their case, the presence of mucin might possibly have been demonstrated by appropriate methods, especially in the papilliferous cystic tumours filled with coagulated fluid. In their clinical history of this case, these writers say that a radiogram of the chest showed a circumscribed area in the upper lobe of the left lung with striations passing from it into the surrounding lung-tissue, an appearance which was interpreted by the radiologist as a possible metastasis; but they further state that this suspicion was not confirmed by the post-mortem findings. They do not, however, give details of any histological examination of the pulmonary lesion. In several of our own cases we should certainly have failed to find the often quite inconspicuous little nodule of bronchial carcinoma, perhaps in connection with a secondary or a tertiary division of a bronchus, had we not previously been convinced that some such tumour must be present because of the naked-eye characters of the multiple cerebral metastases, or from the microscopical findings in the puncture-fluids obtained from the larger mucus-containing cysts which were often present. The old routine method of examining a lung at autopsy by a single slice from the outer side to the root may perhaps reveal even a comparatively small tumour if it chances to be situated in one of the primary bronchi at or near the root, or, if situated at the periphery of the lung where the tumours are often larger and more easily found; but, except for a lucky chance, the plane of section is almost certain to miss a small and sometimes single nodule of tumour if such be present in the body of the lung farther from the hilum. A search for the possible presence of this small tumour may demand a combination of careful palpation with the fingers and the laborious slitting up of the bronchi seriatim from the root outwards into all the lobes of the lungs. In cases of multiple tumours of the brain it is a wise precaution, even if nothing obvious is found in the lungs at the post-mortem itself, to preserve these organs for further detailed examination. Where nodules or patches of old fibrotic change due to pneumoconiosis (the occupation of one of our patients was that of plasterer), chronic tuberculosis, or old syphilitic interstitial pneumonia are present, the difficulty of finding a small nodule of tumour is greatly increased. From our more recent experience of searching for some such very small tumour in the lung, we are by no means surprised that we may ourselves in the past have missed finding them, or that the presence of a small bronchial tumour has not been detected in many of the cases in the literature of multiple cerebral tumours which have not infrequently, we believe, been erroneously described and recorded as 'malignant papillomatous tumours of the choroid plexus.' References to other cases are given in Hall and Fentress' paper,[14] but, on looking up the original articles, a similar suspicion as to their having been in reality metastases from carcinoma of the

lung, or less probably from some other site of origin, arises in one's mind. The literature is so full of such cases that we cannot refer to them in detail, but two further difficulties in connexion with many of the records also call for passing notice. In some otherwise excellent papers upon pulmonary and mediastinal tumours, whether described as papillomatous or 'oat-celled' sarcomatous growths, there is in the majority of the cases no note of the brain having been examined; from the opposite point of view, post-mortem examinations limited to the head may lead to similar fallacious findings from lack of any data as regards the possible presence of some primary tumour in the lung, breast, prostate, gastrointestinal canal or elsewhere.

Of surgical writers on the subject, Percival Bailey of Chicago is one of the comparatively few who seem to be fully alive to the fact that, in the case of elderly patients, especially males, the headache, confusion and other symptoms suggestive of cerebral tumour are not infrequently due to the presence of metastases, often multiple, secondary to tumours in distant organs, and on p. 355 of his recent book *Intracranial Tumors* he [7] writes :—

> 'Primary bronchogenic carcinoma of the lung so commonly metastasizes to the brain, and does it so often before the primary tumour has given symptoms, that it should always be looked for in any patient of middle age, or beyond, who develops rather rapidly symptoms of an infiltrating tumour of the brain, especially if the signs of intracranial hypertension are not marked or there is a pronounced mental confusion.'

On p. 361 he also makes the statement, with which we entirely agree, that :—

> 'The primary pulmonary tumour in its early stages is difficult to recognize, and may have remained entirely symptomless, until after the cerebral metastases are well developed. And these tumours are so numerous that any patient who develops symptoms of intracranial tumour rather rapidly in middle life or later should have a careful examination of the chest, including a roentgenogram, whether pulmonary symptoms are present or not.'

Carcinomas of the lung have been described as occurring in three forms—nodular, lobar, and diffusely infiltrating—but for our present purpose and with regard to the primary focus in the lung, our own series of cases falls conveniently into three main types as follows :—

I. Sclerosing bronchial type, usually at or near the root of the lung.

II. Primary growth, often small, occurring in connexion with a secondary or tertiary bronchus.

III. Larger and sometimes massive tumour at the periphery of the lung.

To illustrate these, we select the following cases :—

I. SCLEROSING BRONCHIAL TYPE

Case I.—J. H. W., age 55, admitted to hospital on September 29, 1933, under the care of Dr. L. R. Yealland, complaining of headache, difficulty in walking and pain in the chest.

History.—Bronchitis on and off for three years with excessive yellow sputum and occasional hæmoptysis, no tubercle bacilli being found. Pain in the chest at times and lassitude for last 18 months. Headache and giddiness for past 12 months and occasional vomiting for six months. His temperament was said to have changed and he had become extremely irritable and at times difficult to manage. No previous illnesses of importance.

Condition on Admission.—Pupils small but equal and reacted normally. Papill-œdema (4D) practically equal on the two sides with small hæmorrhages in the neighbourhood of the disc. Slight nystagmus to left. Other cranial nerves normal. No definite sensory loss. Right armjerks increased as compared with left. Spasticity of both legs about equal on the two sides. Knee- and anklejerks brisk and about equal. No ankle clonus. Plantars—right extensor, left flexor. Abdominal reflexes present and equal. Gait somewhat ataxic but coordination otherwise normal.

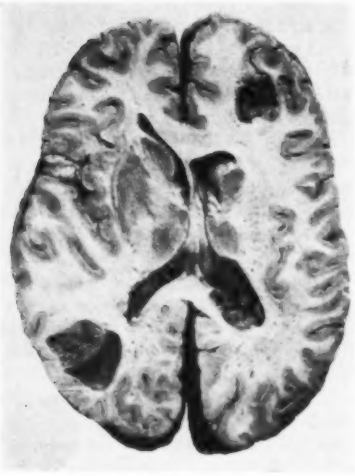
Heart normal. Blood pressure 110/70. Respiration slow but equal on the two sides. Impairment of percussion note at apex of right lung with patchy bronchial breathing. Generalized crepitations and rhonchi over chest.

Cerebrospinal fluid : Small lymphocytes 2 per c.mm. Total protein 0·08 per cent. Globulin a trace in excess. Wassermann and Kahn reactions negative. Lange's colloidal gold curve 0012100000.

Subsequent Progress.—The patient became increasingly drowsy and died 11 days after admission without further change beyond the development of weakness of the lower half of the right side of face.

Post-mortem Examination.—Body extremely emaciated. Dura firmly adherent to inner surface of skull-cap, with some exaggeration of the para-sagittal Pacchionian bodies. The cerebral convolutions were much flattened, and, at the centre of the outer border of the under surface of the left temporo-sphenoidal lobe, there was a large tumour coming to the surface, where it measured 30 mm. × 30 mm., about the size of a small tangerine orange. It occupied the greater part of the interior of the left temporosphenoidal lobe, its surface being level with the general surface of the brain and showing a somewhat lobulated or puckered appearance, rather resembling miniature convolutions, but, on section, showing a fine spongy texture, light greyish brown in colour, and tending to crumble on being cut, its general appearance being much like that of the choroid plexuses. Its margins were fairly discrete and it was easily broken away from the surrounding brain tissue but tending to leave a thin crumbling layer of tumour attached to the latter. On a series of horizontal sections of the brain being made, fairly numerous similar but smaller tumours—some two dozen in all—were found, varying in size from a hazelnut downwards. These were situated in both occipital and both frontal lobes, in both cerebellar hemispheres and elsewhere. The most interesting tumour, however, was found in connexion with the postero-superior wall of the body of the right lateral ventricle, which it was invading, being also continuous in front with, and very much resembling in texture, the hyperplastic right lateral choroid plexus (see fig. 1).

In connexion with some of these tumours, cysts had developed, many of them numerous and of small size but here and there larger, e.g. that shown in the white matter of the left occipital lobe (fig. 1). These cysts were

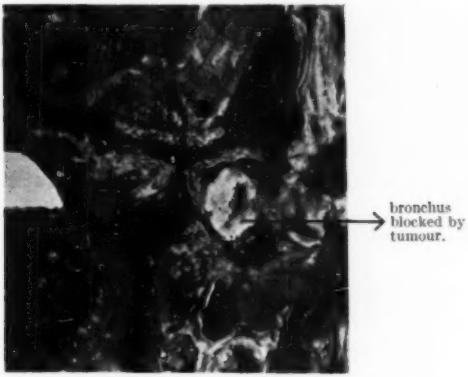


CASE I.

FIG. 1.—Horizontal section through the hemispheres showing several of the metastatic papillomatous tumours—one of them in continuity with the hyperplastic right lateral choroid plexus, invading the ventricular wall and corpus callosum. The nodule in the left occipital lobe shows the development of a cystic cavity not part of the ventricle. This photograph illustrates the appearances which simulate and may be mistaken for malignant papillomatous tumour of the choroid plexus itself.

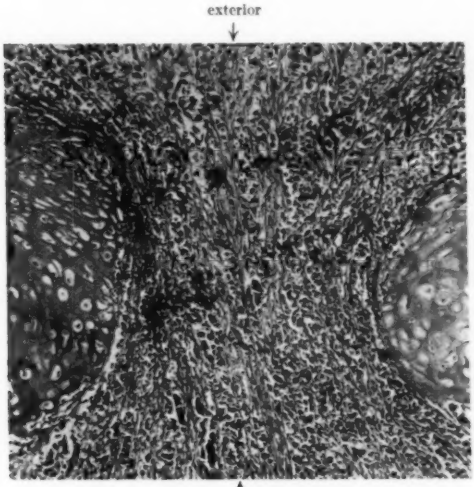
CASE I.

FIG. 2.—Horizontal section through cerebellum, showing numerous secondary nodules of the spongy papillomatous tumour. In connexion with the largest of these growths several cysts of considerable size have developed, the contents of which much resemble mucoid sputum.



CASE I.

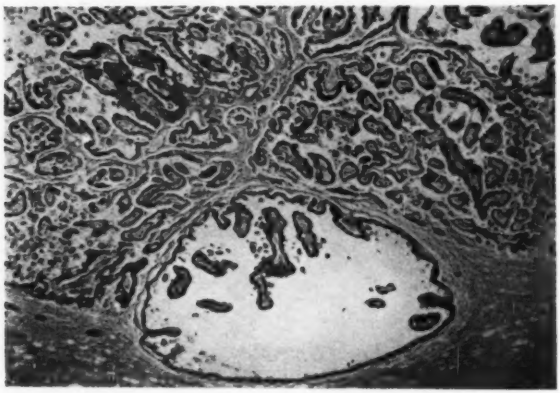
FIG. 3.—Section through the upper lobe of the right lung showing the eparterial bronchus blocked with tumour. The surrounding whitish tissue is mostly fibrotic, of older standing than the neoplastic condition. Immediately above and to the left of the blocked bronchus is a recently thrombosed branch of the pulmonary artery, above and below which are enlarged carbon-pigmented lymph-nodes also containing secondary tumour growth.



CASE I.

FIG. 4.—A low power photograph showing the malignant papillomatous tumour arising from the bronchial mucous membrane, filling the lumen and infiltrating outwards through the wall of the bronchus between two of its cartilages. van Gieson and hæmatoxylin. × 100.

filled with thick colourless and comparatively clear mucoid-looking material, like raw white of egg, swelling and becoming somewhat opaque on fixation with formalin. The largest of these cysts was found in the left cerebellar hemisphere, measuring slightly over 30 mm. in its greatest diameter, the adjoining tumour from which it had developed and several smaller cysts being shown in fig. 2, in which several other smaller nodules of spongy tumour are shown in both cerebellar hemispheres and also in the choroid plexus of the fourth ventricle. The various choroid plexuses were voluminous and hyperplastic, their appearance being somewhat suggestive of the ' villous hyper-



CASE I.

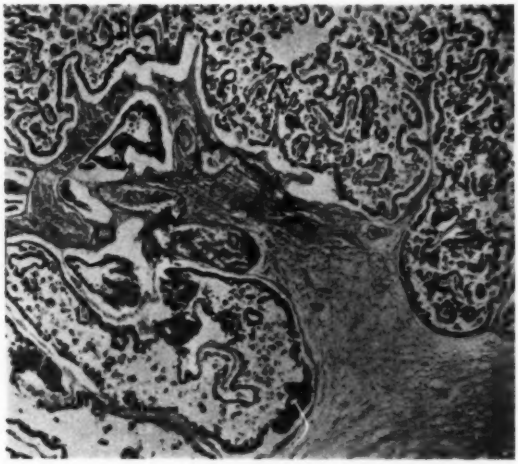
FIG. 5.—Low power of spreading margin of tumour in right frontal lobe, showing the combined cystic and papillomatous structure. Mallory's stain for connective tissue. × 32.

trophy ' described by L. E. Davis [15] in 1924 as occurring in many cases of hydrocephalus.

In the thorax there were firm old fibrous adhesions of the right lung to the chest wall, especially over the upper lobe and its junction with the middle lobe. On palpating the root of the right lung, there was a firm nodulated mass suggestive of possible tumour, but found to be due mainly to an old fibrotic condition spreading outwards into the lung-tissue from the root. On dissection, the eparterial bronchus was found to be the seat of a stenosing carcinoma (fig. 3), and the surrounding lung-tissue showed a mixture of fibrosis resembling a silicosis (the patient's occupation had been that of plasterer) and the infiltrating malignant tumour. A few small, firm, pea-like nodules, found microscopically to be a mixture of fibrosis and tumour, were also scattered elsewhere in the lower part of the upper lobe and in the middle lobe. No caseation or other evidence of tuberculosis could be made out with the naked eye. Several moderately enlarged lymph-nodes at the root

showed a mottled mixture of opaque white metastatic tumour and black carbon-pigmented fibrotic tissue. The whole of the upper lobe was collapsed, congested and intensely œdematous, and there was recent thrombosis of the larger branches of the pulmonary artery to this lobe. The rest of the right lung and also the left lung showed chronic bronchitis with thickening and peribronchial fibrosis and scattered small nodules of tumour. The right lower lobe and most of the left lung also showed marked emphysema.

The heart was extremely soft and flabby, its chambers dilated and the myocardium showing a mixture of fatty degeneration and brown atrophy



CASE I.

FIG. 6.—Low power view of the nodule of tumour involving the choroid of the right lateral ventricle and the neighbouring portion of the ventricular wall. The general appearance of the tumour was suggestive of choroid plexus, from which it was at first believed to have originated. Hæmatoxylin and eosin. × 32.

with a considerable degree of atheroma of the aorta, aortic cusps and coronary arteries, especially the right.

Abdomen.—Except for one small nodule of tumour, 4 to 5 mm. in diameter, in the medulla of the left suprarenal, opaque pearly-white in colour and slightly granular when its cut surface was examined with a hand-lens, no metastases were found, the suprarenal itself not being appreciably enlarged. The liver and kidneys showed merely fatty degeneration and chronic venous congestion and the only other abnormality found was a moderate-sized hydrocele of the right testicle, with no naked eye evidence of tumour.

Microscopically.—The lumen and walls of the right eparterial bronchus, just as it entered the lung tissue, and its main branches were the seat of a

malignant papillomatous tumour arising from the bronchial mucous membrane (fig. 4). In some parts of its structure, the tumour was loose and 'feathery,' in others more densely packed, and, where it was invading already fibrosed lung-tissue, almost resembling a scirrhus cancer in structure. Most of the latter areas showed marked increase of carbon and also the presence of particles of stone-pigment, this condition having probably preceded the occurrence of the tumour and being apparently of the nature of a silicosis. In some of these areas there was also a considerable degree of chronic

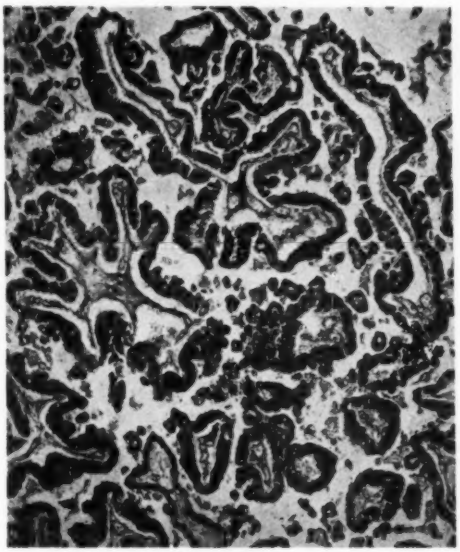
CASE I.

FIG. 7.—Low power view of the spreading margin of the tumour involving the right lateral choroid plexus, showing the general papilliferous structure of the tumour. The outermost layer of columnar epithelium is, however, suggestive of its bronchial origin, and when stained with mucicarmine, gives the specific stain for mucin. At the infiltrating margins, the tumour appears to carry outwards its own delicate connective-tissue stroma and blood-vessels, many of which show a dilated sinus-like structure. Hæmatoxylin and eosin. × 100.

irritation—small round-celled infiltration with lymphocyte-like cells. The secondary growth in the bronchial glands gave a similar picture, the looser 'feathery' papillomatous characters being best seen where papilliferous cysts had developed, and in other parts the tumour-cells being mixed with much carbon-pigmented and fibrotic tissue. The small nodule in the left suprarenal also consisted of typical malignant papilloma.

As we are writing from the neurological standpoint, the histology of the multiple malignant tumours in the brain may be described a little more fully, and this is most satisfactorily done by referring to the accompanying illustrations and their annexed descriptions. Figs. 5, 6, 7 and 8 are low-power

microphotographs of the spreading margins of the nodule of secondary growth involving the choroid plexus and wall of the right lateral ventricle and show appearances which might easily mislead one into the belief that the tumour had actually arisen as a primary tumour of the choroid plexus itself. This is perhaps particularly so in the case of fig. 6. Fig. 8 is more suggestive of a tumour arising from a mucous membrane or a gland lined by columnar epithelial cells, and, when the tissue was stained with mucicarmine, the presence of mucin, which would naturally not be present in a tumour arising from the choroid plexus, could be demonstrated in it. Figs. 5 and 6 show the tendency to the formation of papillomatous cysts, which may



CASE I.

FIG. 8.—Low power view of a secondary nodule in the frontal lobe, showing a typical metastasis of the bronchial papillomatous carcinoma. van Gieson and hæmatoxylin. × 100.

vary in size from microscopic up to large naked-eye cysts such as those shown in figs. 1 and 2.

Although *blepharoplasten* might be expected in cells derived from the originally ciliated bronchial epithelium, we were unable, by Bailey's neutral ethyl violet orange G, and other special methods, to demonstrate their presence in the papillomatous cells of the tumours either in the brain or in the lung itself, and we are therefore not inclined to stress a negative finding in this respect as of great importance. Similarly no cilia were themselves detected at the free margins of any of the cells.

II. SMALL AND INCONSPICUOUS GROWTH IN RELATION TO A SECONDARY BRONCHUS

Case II.—A. S., male, age 47, was admitted to hospital on December 29, 1934.

History.—He had felt quite well until two months previously, viz. October 1934, when he became rather quiet in manner and seemed tired, especially in the mornings. No complaint of headache at that time. A month before admission he had stopped working because he felt ill but had no very definite complaint. His appetite then failed and his speech became vague and indistinct: he made irrelevant answers and seemed at times to be rather confused and complained of severe headache. At the same time he had several painful boils, the largest being on the neck and at the vertex of the head.

Condition on Admission.—Pupils central, equal and reacted to light and on accommodation. Both fundi showed papilloedema. No nystagmus. Slight weakness of lower half of face on right side. Some degree of aphasia. Sensation as far as could be tested appeared normal. Upper limbs: normal. Right leg spastic, kneejerks exaggerated and right anklejerk greater than left. Double extensor plantar response. Right lower abdominal reflex absent. With finger-nose test some ataxia on right side. Sphincters: double incontinence.

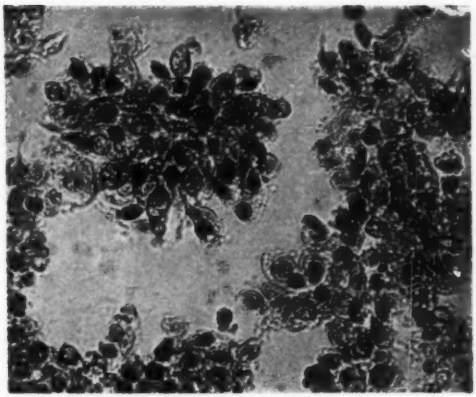
Heart normal, blood-vessels not thickened. Blood pressure 130/96. Respiratory system: an area at the base of right lung showed increased resonance with loud expiration and impaired percussion note. X-ray examination of chest: no abnormality detected. Cerebrospinal fluid showed pressure 170 mm. Queckenstedt test normal. Cells: 3 small lymphocytes per c.mm. Total protein 0·05 per cent. Globulin faintest detectable trace. Wassermann and Kahn reactions negative. Lange's colloidal gold curve 0121000000. Blood Wassermann and Kahn reactions negative.

Blood: leucocytes 8,200 per c.mm. Films showed moderate but distinct anisocytosis, but otherwise nothing of note.

Subsequent Progress.—A lesion of the left frontoparietal region was diagnosed. The physical signs in the right lung, though scanty, suggested the possibility of a bronchial carcinoma, and an X-ray examination was carried out. This however was reported negative. In view of the recent history of several boils the possibility of cerebral abscess was also considered and, as the papilloedema was increasing, a left-sided subtemporal decompression was carried out by Mr. C. P. G. Wakeley. Death occurred two days later on January 7, 1935.

Post-mortem Examination.—The body was poorly developed and showed considerable emaciation.

On opening up the recent left-sided subtemporal decompression area there was considerable flattening of the cerebral convolutions, the temporo-sphenoidal lobe on this side having a 'baggy' feeling and appearance. Some turbid fluid aspirated through a needle after deep insertion in this region and examined in fresh wet preparations (see fig. 9) showed numerous obviously malignant tumour-cells, mostly small and rounded in shape, but sometimes oat-shaped, and occasionally somewhat columnar. Several clumps of cells showed a suggestion of radial arrangement, such as one might expect in a papillomatous tumour, but with no trace of any connective-tissue cores. These were sufficiently suggestive of the structure found in some other cerebral metastases from bronchial tumours to warrant a provisional diagnosis of 'metastases (probably multiple) in the brain from a primary bronchial



CASE II.

FIG. 9.—Fluid aspirated from cystic tumour in temporosphenoidal lobe. A fresh wet preparation stained with methylene blue showing clumps of epithelial cells, suggesting fragments of papillomatous tumour. Some of the cells are oat-shaped, others small-round. From these and other similar preparations a diagnosis of malignant tumour (probably multiple) secondary to a bronchial carcinoma was suggested. Methylene blue. × 400.

CASE II.

FIG. 10.—Horizontal section of the cerebral hemispheres above the level of the corpus callosum. A metastatic tumour of considerable size is seen in the outer and posterior part of the left frontal lobe.

carcinoma,' this being confirmed by the further examination of the brain after removal and fixation. At the level of the upper surface of the corpus callosum, in the left frontal lobe and occupying its posteroexternal portion there was an irregularly rounded tumour, the size of a walnut, mainly in the white but also encroaching upon the inner aspect of the grey matter (fig. 10). The cut surface of this tumour showed the distinct spongy and crumbling character suggestive of a papillomatous tumour secondary to bronchial carcinoma. The central portion of the tumour also showed some patchy yellow necrosis and in its lower part there were some small mucus-containing cysts. In the temporosphenoidal lobe there was a similar but rather smaller tumour showing the same spongy texture and the presence of a considerable

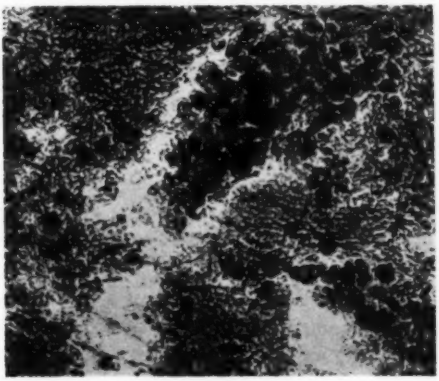
CASE II.

FIG. 11.—Naked-eye photograph of left lung, showing the two cut halves of a small primary bronchial carcinoma on one of the main branches of the bronchus to the upper lobe. The tumour is only about the size of a pea, but is surrounded by some chronic induration and fibrosis.

amount of thick sputum-like mucus, from the aspirated contents of which the provisional diagnosis of tumour secondary to bronchial carcinoma had been made. A third nodule, about the size of a marble (15 to 20 mm. in diameter) was found in the centre of the right cerebellar lobe, mainly amongst the leaves of grey matter.

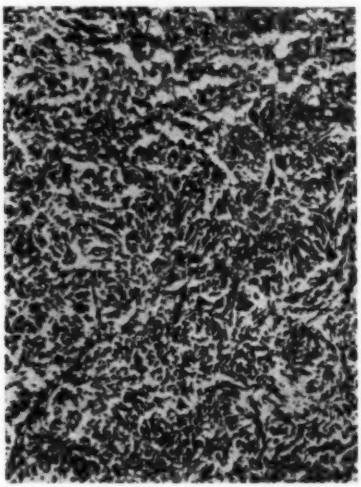
The heart was extremely soft, flabby and atrophied, with marked fatty infiltration of the right ventricle, the myocardium of the left ventricle being also atrophied and showing fatty degeneration. The coronary arteries showed distinct thickening and patches of atheroma.

Both lungs showed a considerable degree of emphysema of their apices and borders. There was well-marked chronic bronchitis with chronic



CASE II.

FIG. 12.—A fresh wet teased preparation of the brain substance at the margin of the temporosphenoidal tumour, showing infiltration by groups of malignant epithelial cells among the glial fibres. Toluidin blue. × 400.



CASE II.

FIG. 13.—Low power view of margin of secondary tumour in temporosphenoidal lobe, showing the loose feathery arrangement of the epithelial cells, somewhat suggestive of a catarrhal bronchitic exudate. Hæmatoxylin and eosin. × 100.

congestion, thinning and catarrh of the bronchial mucous membrane, with also some slight, more or less diffuse dilatation of many of the smaller bronchi.

In the left lung there was found, in the upper part of the lower lobe, a

small hard firm nodule-like mass, about the size of a small pea, situated about 2 inches from the root. This had the appearance of a small nodule of tumour in connexion with a medium-sized bronchus and around this nodule was some radiating fibrosis and carbon-pigmentation (fig. 11).

The bronchial and other mediastinal lymph-nodes showed congestion and some excess of carbon-pigmentation, but no obvious naked-eye evidence of tumour.

No nodules of new growth were found in the liver, spleen, pancreas, kidneys, gastrointestinal tract, bladder or prostate, or in any of the lymph-nodes.

Microscopically.—Teased fresh wet preparations of the brain-substance from the margins of the temporosphenoidal tumour (fig. 12) showed small groups of infiltrating malignant epithelial cells among the glial fibres, etc., and, as already noted above, the mucoid fluid aspirated from the cystic portions of this tumour also showed epithelial cells the characters of which suggested that they were derived from a papillomatous bronchial or other carcinoma.

Sections of the small primary bronchial carcinoma itself (fig. 13) showed the epithelial cells arranged in a loose, 'feathery' manner, with, here and there, a suggestion of papillomatous structure, but most of the cells were oat-shaped to slightly columnar. The same loose feathery arrangement of the epithelial cells was found in sections of the temporosphenoidal tumour, in some parts almost suggestive of a 'catarrhal bronchitic exudate'; while in other metastases, e.g. that in the frontal lobe, the papilloma-like structure was more in evidence.

III. MASSIVE PRIMARY GROWTH AT PERIPHERY OF LUNG

Case III.—G. A. W., male, age 56, admitted to hospital on July 5, 1934.

History.—This patient had been seen and examined by one of us in January 1926—over nine years before. He was then complaining of lack of mental concentration and shakiness on excitement, of four months' duration. He showed no evidence of organic disease either of the nervous or other systems. The heart was normal and blood-pressure 140/80. The blood gave a weak positive Wassermann reaction.

He was then lost sight of until the day before his admission to hospital.

Condition on Admission.—Mentally confused, used words in their wrong places and had little or no memory for recent events. He stated that he had no complaints excepting headaches which he 'had had for years.'

Pupils: small but equal, reacted normally. Bilateral papillœdema (1·5 D). Slight nystagmus to left. Other cranial nerves normal. Upper limb reflexes brisk and equal. Right knee- and anklejerks greater than left. Plantars: right extensor, left indefinite. Abdominal reflexes absent. Incoordination of right arm. Heart normal, blood-pressure 118/70. Some dulness over upper lobe of left lung with diminished breath and voice sounds. Cerebrospinal fluid: 26 cells per c.mm., practically all small lymphocytes with an occasional small endothelial cell. Total protein 0·06 per cent. Globulin: a trace in excess. Wassermann reaction weak positive. Lange 5553210000. Blood Wassermann reaction weak positive.

Subsequent Progress.—The patient became increasingly confused, drowsy and

incontinent. Death occurred a few days after admission. The fact that this patient was undoubtedly a syphilitic subject and probably suffering from early dementia paralytica obscured the diagnosis. The chest condition was suspected on account of the physical signs but his mental condition precluded an X-ray examination.

Post-mortem Examination.—The body, unlike that of our other cases in which emaciation was a notable feature, was well developed and well nourished with distinct excess of adipose tissue.

Head.—The skull-cap was dense and heavy and to it the subjacent dura was firmly adherent. The whole brain was extremely soft and its convolu-

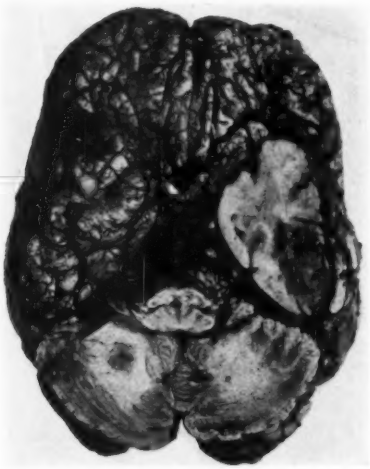
CASE III.

FIG. 14.—Horizontal section through cerebral hemispheres, showing two large coalescing metastatic nodules of the bronchogenic carcinoma in the left frontal lobe, etc. The choroid plexuses of the lateral ventricles show well-marked hyperplasia.

tions much flattened. The left frontal lobe showed a condition of 'baggy softening' with breaking down of the cerebral substance anteroexternally. During removal, a large soft necrotic dark reddish mass of tumour mixed with bloodclot began to protrude at this area, and the whole brain was at once placed in fixative.

On horizontal section after fixation, two large coalescing masses of malignant tumour were found infiltrating and replacing most of the left frontal lobe and the area of the caudate nucleus, etc. (fig. 14), producing great bulging of the anterior half of the left hemisphere and pushing some of its structures well beyond the middle line to the left and also backwards. The anterior and larger mass of tumour had a loose necrotic spongy texture with extensive hæmorrhage into it. The smaller posterointernal mass was

somewhat whiter in colour but also finely spongy to granular in texture, and also showed patchy hæmorrhages. The lateral ventricles showed considerable dilatation—the right as a whole, the left only above the level of the tumour which bulged into the roof of its anterior horn, the interior of which was invaded. Another considerable mass of tumour was found in the postero-external and inferior aspects of the left temporosphenoidal lobe and a smaller metastasis about the size of a hazelnut was present in the central white matter of the right cerebellar hemisphere (fig. 15). These showed a varie-



CASE III.

FIG. 15.—Base of the brain with portions of left temporosphenoidal lobe and cerebellum cut away, showing large metastatic tumour in the former, and smaller nodule in the centre of the right lobe of the cerebellum.

gated, somewhat granular, whitish and pinkish-white appearance mixed with hæmorrhage and some necrosis.

The heart was small, soft and flabby, and showed an extreme degree of fatty infiltration, especially of the right ventricle, with marked atheroma of the aorta and coronary arteries and patchy thickening of the aortic cusps and anterior cusp of the mitral valve.

Both lungs were extremely œdematous and congested and, in the lower part of the upper lobe of the left lung, there was a large firm nodular mass about the size of a medium-sized orange (fig. 16), over which there was old dense fibrous thickening of the pleura, but without adhesion to the chest-wall.

On section, this mass showed a granular, yellowish-white necrotic appearance throughout its central part, but at the periphery it was less opaque and showed a zone of pinkish-white tumour-like tissue. This was the

only mass suggestive of tumour growth in the lungs, nothing being detected towards the roots indicative of neoplasm.

In the abdomen, there was a small secondary growth, about the size of a pea, in the spleen immediately beneath the capsule on the diaphragmatic surface towards its upper pole. No nodules of tumour were found in the liver, but in and greatly distending the left suprarenal body was a soft mass of tumour about the size of a small orange. A minute metastasis was found in the right suprarenal, but none in the pancreas or kidneys.

CASE III.

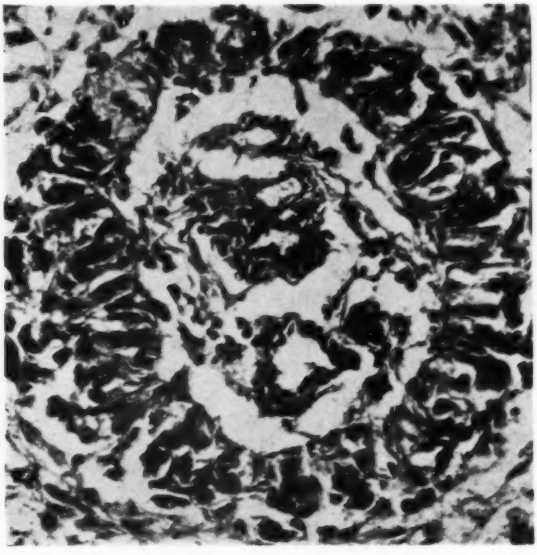
FIG. 16.—Naked-eye photograph of the primary tumour in the lower part of the upper lobe of the left lung.

Microscopically.—The histological appearances in sections of the primary lung tumour and of the metastases in the brain and suprarenal, etc., were all practically identical, the epithelial cells being loosely arranged in feathery masses and the individual cells often separated from one another by clear mucoid fluid. These cells, even in section, showed an appearance suggestive of the exudate of an acute catarrhal bronchitis. All the tumours showed numerous patchy areas of necrosis and hæmorrhage, the surviving tumour-cells being arranged in zones immediately around the numerous, rather

delicate, thin-walled blood-vessels, which were sometimes dilated and sinus-like. Some of these phenomena were perhaps associated with the pre-existing syphilitic element in this case.

The three foregoing cases may be taken as representative of the three groups into which we have divided the cases of bronchogenic carcinoma which we have encountered. We give, therefore, only a brief synopsis of our remaining cases and need refer only to some of the points in which they differ from the cases already described.

Case IV.—A. A., male, age 64. This patient was under the care of Mr. C. P. G. Wakeley. There was a clinical history of inability to concentrate and loss of memory, with vomiting and failure of vision. He was admitted to hospital (January 4, 1934) in a condition of stupor.



CASE IV.

FIG. 17.—High power view of margin of tumour showing the surrounding brain tissue invaded by a papilloma-like process, with central vascular core and radially arranged bronchial epithelial cells. Hæmatoxylin and eosin. × 400.

The physical signs pointed to the presence of a cerebral tumour of the right parietal lobe. A large right temporal decompression was performed and an inoperable tumour found in the temporosphenoidal lobe. After some temporary improvement, the patient died six weeks later.

Post-mortem Examination.—(Limited to head.)—*Brain.*—The right cerebral hemisphere was much larger than the left and showed large spongy metastatic growths in the temporosphenoidal and frontal lobes.

Microscopically.—These tumours showed the feathery and papillomatous appearances characteristic of bronchogenic carcinomatous metastases which are illustrated in fig. 17.

Case V.—H. S. H., male, age 45, admitted under the care of Dr. L. R. Yealland with symptoms of cerebral tumour—severe headaches, failure of memory and gradually increasing coma, death occurring about a fortnight after admission.

Post-mortem Examination.—(Limited to head.)—A poorly developed and somewhat emaciated adult male. Marked general flattening of the cerebral convolutions with ' baggy ' softening and bulging in the centre of the

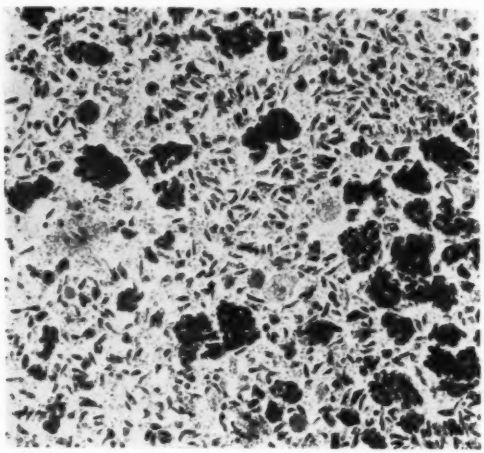
CASE V.

FIG. 18.—Horizontal section through the cerebral hemispheres, showing some of the spongy metastatic growths.

outer surface of the right temporosphenoidal lobe, in which there was a large spongy and extensively cystic metastatic malignant tumour which had burrowed downwards and inwards and had become adherent to the upper surface of the tentorium cerebelli about its centre (figs. 18 and 19). Some of the contents of this, aspirated for immediate examination, were mucoid and sputum-like and, microscopically, showed numerous columnar or cigar-shaped epithelial cells suggestive of a bronchitic exudate, together with little clumps of cells, evidently fragments of papillomatous tumour, from which the provisional diagnosis of a bronchial carcinoma was made (fig. 20). On serial horizontal section, about a dozen soft spongy tumours were found throughout the brain, varying in size from that of a pea up to that of a tangerine orange, the largest being that already described, in which cystic projec-

CASE V.

FIG. 19.—Under surface of horizontal section through the cerebral hemispheres, showing some of the spongy metastatic growths. That on the left side posteriorly in the occipital and temporosphenoidal lobes is, at a lower level, extensively cystic, and from it the 'catarrhal' and sputum-like fluid shown in fig. 20 was obtained.



CASE V.

FIG. 20.—Fresh wet contents of a large cystic tumour in the inner part of the substance of the left temporosphenoidal lobe, which burrowed towards the pineal region, where it became adherent to the tentorium cerebelli. The aspirated contents of this were mucoid and resembled sputum in consistency and appearance. Microscopically, as shown here, it suggested an admixture of small fragments of papillomatous tumour and bronchial catarrhal cells. Toluidin blue. × 100.

tions from the lower part of the occipital and temporosphenoidal lobes were found. There was also a smaller nodule in the left lobe of the cerebellum, among the cortical leaves, towards its posterointernal part.

Case VI.—E. W., male, age 61, admitted under the care of Dr. L. R. Yealland in January, 1933, complaining of diminishing vision and headache.

History.—He was stated to have been well until five months previously to admission when he had a 'stroke' and 'saw coloured lights,' with impairment of

CASE VI.

FIG. 21.—Under surface of a horizontal section through cerebral hemispheres showing the large metastatic tumour invading the right occipital lobe, pushing its way forwards and compressing the posterior horn, the posterior part of which is seen as a slit-like cavity in front of it towards the middle line. The tumour has also burrowed its way forwards into the body of the right lateral ventricle as far as the origin of the descending horn. An irregular nodule of the tumour is also seen in connexion with the anterior horn of the same ventricle, showing the development of a cyst-like cavity filled with mucus. A smaller subcortical nodule is seen on the left side, towards the posterior part of the parietal lobe. (Note.—This is a photograph of the *under* surface of this portion of brain and the sides therefore appear reversed.)

sight on looking to the left. He suffered from frontal and occipital headaches—the former mostly on the right side.

Condition on Admission.—Pupils small, central but irregular. Reaction to light normal. The right visual field was slightly diminished to the right, the left absent on the left as far as the fixation point. The fundi showed papillœdema.

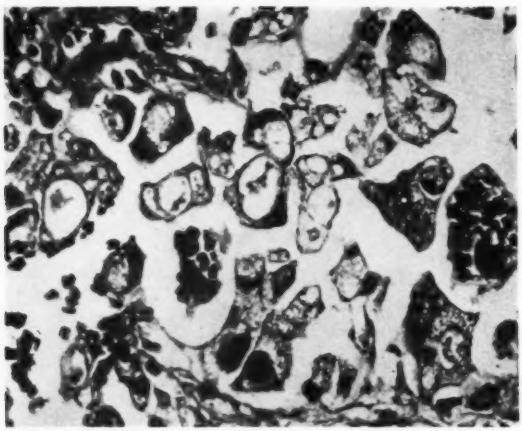
The cerebrospinal fluid showed a slight, but distinct, yellowish tint but no frothing. Cells 2 per c.mm.—small lymphocytes. Total protein 0·12 per cent. Globulin in slight excess.

Lange 0012210000. Wassermann and Kahn reactions negative, as also in the blood. A leucocyte count gave 15,300 per c.mm. (polymorphs 68·5 per cent.; lymphocytes

13·0 per cent.; monocytes 18·5 per cent.; eosinophils and basophils 0·0 per cent.). Blood urea 51 mgm. per cent.

Progress.—The patient grew steadily worse, developing patchy dulness in the lung with much secretion, which he was unable to expectorate. He became very emaciated, with frequent attacks of vomiting and further deterioration of vision, death occurring on May 13, 1933. The provisional diagnosis was one of right occipital lobe tumour.

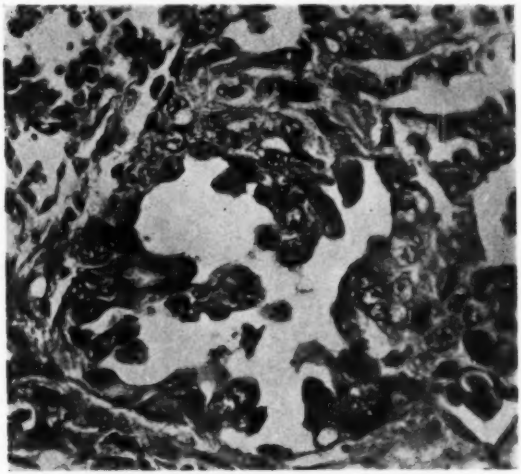
Post-mortem Examination.—As shown in the accompanying photograph (fig. 21), a large malignant tumour was found occupying most of the right occipital pole. On section, this was variegated in appearance, some parts



CASE VI.

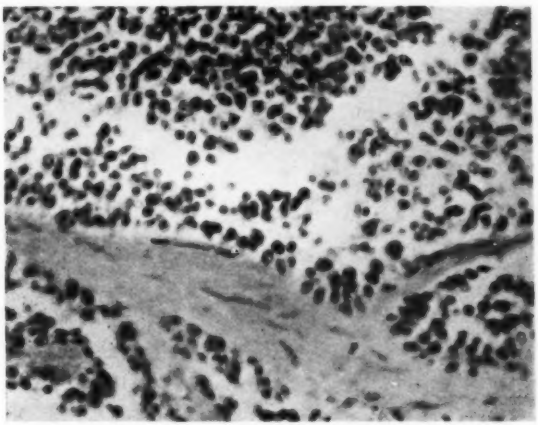
FIG. 22.—Occipital tumour: high power view showing the actively phagocytic and highly vacuolated tumour-cells, some of which contain numerous englobed red blood corpuscles. Some of the larger vacuoles when empty simulate the appearance of transverse sections of capillaries, with the nucleus stretched and pushed to one side and the cytoplasm reduced to a thin peripheral ring. Hæmatoxylin and eosin. × 400.

being pearly rather opaque white, others dark red and hæmorrhagic, and yet others showing old-standing blood-pigmentation together with mottled areas of necrosis. The tumour was much firmer than the surrounding brain-tissue and did not show the crumbling spongy appearance of the majority of our cases of bronchogenic carcinoma—perhaps because of the distinct tendency to reversion to squamous epithelium. Anteriorly, this tumour involved the posterior horn and body of the right lateral ventricle, being continuous with the choroid plexus. Another fairly large nodule with considerable cystic development was found in connexion with the anterior horn of the same ventricle, while a subcortical nodule was present on the other side towards the junction of parietal and occipital lobes.



(Dr. Norah Schuster's Case.)

Fig. 23.—High power view of portion of infiltrating malignant tumour of the bronchial mucous membrane, showing the tendency to reversion to squamous epithelium, lining cystic spaces with papillomatous ingrowths into them. Mayer's mucicarmine. × 400.



(Dr. McMenemey's Case.)

Fig. 24.—High power view of metastasis in suprarenal, showing the small round-cells which gave rise to the diagnosis of small round-celled sarcoma. The spaces, however, are lined at the periphery by epithelial cells similar to those found upon the papillomatous processes seen in sections of the primary lung tumour and the cerebral metastases from it. Hæmatoxylin and eosin. × 400.

The microscopical appearances are shown in fig. 22. The chief interest of this case lay in the fact that, although some parts of the tumour were distinctly papillomatous in structure, there was a tendency of the tumour-cells to show a reversion to a squamous type of epithelium, a metaplastic change not uncommon in the primary bronchial carcinomas themselves. The individual cells of this tumour were highly phagocytic, not only to red blood-corpuscles and leucocytes, but also to other tumour-cells, the remains of which, in all stages of digestion, could be found in the digestive vacuoles (see fig. 22). When stained by Mayer's mucicarmine method, numerous globules and granules of mucin could be demonstrated in the cytoplasm of the cells, particularly in those which had been englobed by other tumour-cells.

It is interesting to note that in three of Schuster's cases varying degrees of this metaplasia to squamous cells were found in some parts of both primary and secondary tumours (fig. 23) which might otherwise have been labelled small round-celled tumours. As a typical example of the latter we show a microphotograph (fig. 24) from the case of a man (age 43), for which we are indebted to our colleague Dr. W. H. McMenemey, who found it labelled with a diagnosis of 'small round-celled sarcoma' among some old microscopical preparations in one of his hospitals. This was from a metastasis in the suprarenal body, similar tumours being found in the lung in which they show characteristically papillomatous structures, the primary tumour being a bronchial carcinoma.

CLINICAL COMMENTARY

It is noteworthy that all our patients were males and came under observation purely on account of cerebral symptoms at a neurological hospital. Their ages varied between 43 and 64 years, the average age being 53. In Levy Simpson's [6] series of 139 cases of bronchial carcinoma the average age was 48; 111 were males and 28 females (four to one). The majority of observers place the ratio as three males to one female affected. Metastases of the brain occurred in 19 of Levy Simpson's 139 cases, and in 11 of the 19 the primary bronchial growth was not detected clinically. In Ormerod's [16] series of 27 cases at Brompton and Westminster Hospitals 23 were in males and four in females. Improved X-ray technique and the use of lipiodol, bronchoscopy and the histological examination of a biopsy specimen have greatly facilitated the diagnosis of such cases.

Chest symptoms were inconspicuous or practically absent in all but two of our cases. One of these patients had complained of a cough for 18 months and the other of a slight cough for only a few weeks. In the former case (sclerosing bronchial type of tumour), suggestive signs were found in the upper lobe of the right lung, but in the second case only a few râles at the bases were apparent. In two other cases signs were detected in the lungs in the absence of symptoms. In one case (Case II) with a small primary tumour on a secondary bronchus, an X-ray examination was carried out with

negative results. The second case (Case III) showed definite signs in the left upper lobe.

When sputum is available from cases of suspected bronchial carcinoma, suitable specimens should be examined for the presence of malignant cells, preferably by fresh wet staining methods, for which purpose we have found toluidine blue one of the most useful dyes.

In all cases headache was a prominent symptom, also mental symptoms such as confusion, lack of concentration, failure of memory and disorientation. In three cases a definite change of temperament was noted.

Papillœdema was found at some stage of the illness in all cases. Nystagmus was present in three, but, apart from weakness of the lower half of one side of the face (as part of a hemiparesis) in two cases, other cranial nerves were not affected. The deep reflexes were unequal in all cases; both plantar reflexes were extensor in four and one in the remainder.

The blood pressure was uniformly low, the highest pressure recorded being 130/96. The latter was also the highest diastolic pressure—in a man of 47. The lowest was 110/65. It is of interest to note that in the two patients with the lowest pressures—110/65 and 118/70—a large metastasis was found in the left suprarenal body in each case.

As regards the cerebrospinal fluid, no definite increase in cells was found in any case with the solitary exception of the patient (Case III) showing evidence of previous syphilis. In this example, 26 small lymphocytes per c.mm. were present, but, in addition, the Wassermann reaction was weakly positive and the Lange reaction showed a curve of paretic type. This increase in lymphocytes, therefore, was more probably a result of the syphilitic infection than of the cerebral neoplasms. Increase in the total protein was only moderate except in one case. In this latter the amount was 0·12 per cent. The lowest was 0·04 per cent., figures from 0·06 to 0·08 per cent. occurring in the remaining cases.

In cases submitted to operation—owing to the exact nature of the tumour being doubtful—there is always the possibility of a definite diagnosis being made by the examination of puncture-fluid aspirated from one of the more superficial cystic tumours (see Pathological Commentary).

In general, the clinical symptoms and signs indicate lesions of the frontal or temporosphenoidal lobes and/or of the cerebellum in which situations the larger tumours were found to occur.

PATHOLOGICAL COMMENTARY

From the pathological standpoint, perhaps the most interesting and important problem in connexion with this series of cases has been the question of excluding the possibility of the diagnosis of choroid papilloma. Many of the cases with this diagnosis described in the literature, especially in middle-aged to elderly patients, in our opinion, have been typical examples of

cerebral metastases derived from a primary bronchial carcinoma. We have already drawn attention to the latency of the symptoms, especially in males.

In our series of cases, the largest of these cerebral metastases have usually been in the temporosphenoidal and frontal lobes and in the cerebellum. We have also emphasized the fact of their presence in, and continuity with, the choroid plexuses themselves in an appreciable number of cases. These are obviously due to the implantation of embolic malignant cells in the choroid vessels. In this connexion it is interesting to recall that an infective disease, meningococcal meningitis, in an analogous manner, probably results from the meningococci being carried by the bloodstream to the choroid plexuses, from which the infection is carried by way of the ventricular chain to the surface of the brain.[17]

Secondary growths of the bronchogenic carcinoma, in almost every case, were also found in the suprarenal medulla, which may from this point of view be regarded as a part of the nervous system.

Histologically, both the primary bronchial carcinomas and the secondary growths in the brain and other organs usually show, in whole or in part, an appreciable and often a marked tendency towards the development of a papillomatous structure. The tumour-cells often retain a considerable capacity for secreting mucus, and cysts of varying size filled with sputum-like material may develop, not infrequently giving a baggy feeling to the overlying surface of the brain. It is often not a difficult matter to obtain some of their contents through a puncture-needle. The presence of fragments of papillomatous tumour and numerous cigar-shaped, columnar or tailed epithelial cells resembling those of a catarrhal bronchitis may facilitate the diagnosis. Mucin may often be demonstrated, whereas in the contents of somewhat similar tumours secondary to carcinoma of the breast we have found numerous fatty granules and globules almost suggestive of an imperfect attempt at milk secretion.*

The naked-eye appearances of the secondary tumours are usually characteristic. They are spongy and friable and are easily enucleated, but leave a thin ragged layer of malignant cells in the wall of the cavity. The tumours in which squamous-celled metaplasia has occurred tend to be firmer in consistency, less spongy, and may show a variegated appearance on section (Case VI).

We have emphasized the great variability of the naked-eye appearances of the primary bronchial tumours in the lungs. Some of these in the larger bronchi near the root or in the lung tissue at the periphery of the organs are easily found, but others in an intermediate position, e.g. in connexion with

* The diagnosis of these and other cerebral tumours, primary and secondary, by means of fresh wet preparations of exploratory puncture-fluids formed the subject of a separate paper communicated by one of us to the Second International Neurological Congress, London, 1935 (*Congress Abstracts*, p. 101).

secondary or tertiary divisions of the bronchi, may be inconspicuous and are easily overlooked.

In conclusion, we desire to thank our colleagues, especially Dr. L. R. Yealland, Dr. T. R. Hill, Dr. W. H. McMenemey, Dr. Norah Schuster and Mr. C. P. G. Wakeley for kindly allowing us to include some of their clinical and pathological material. Also, we have to acknowledge the valuable technical help of Messrs. J. Ottewill and K. Osborne and of Miss M. I. Wilson in the laboratory.

SUMMARY

1. Cases of multiple metastatic tumours of the brain secondary to primary bronchial carcinoma are described and analysed. As regards the primary focus in the lung, the cases fall into three main types : (1) sclerosing bronchial growth, (2) primary growth in connexion with a secondary or tertiary bronchus, and (3) large tumour especially at the periphery of the lung.

2. The increased incidence of such cases in recent years, the latency of symptoms of the primary bronchial focus and the liability for cerebral symptoms to dominate the clinical picture in males are confirmed.

3. In the brain, metastases are liable to occur especially in the frontal and temporosphenoidal lobes and in the cerebellum. The suprarenal medulla is also a frequent site of such secondary growths.

4. The symptoms include headache, mental confusion, defects of memory and occasionally a change of temperament. Papillœdema is invariably present, together with changes in the deep reflexes of the limbs and an extensor plantar reflex—bilateral or unilateral.

5. We emphasize the definite tendency for bronchogenic carcinoma, both primary and secondary, to be papillomatous in its histological characters.

6. Attention is drawn to the frequent occurrence of metastases in the choroid plexuses. From a perusal of the literature, we consider that many cases in which this has occurred have been described erroneously as examples of malignant papilloma of the choroid plexus.

7. Cysts often develop in connexion with the cerebral metastases, and these usually contain mucin, tests for which materially assist in the diagnosis.

8. The observation is made that puncture-fluids aspirated from such cysts may resemble sputum and that fresh wet films may show fragments of the papillomatous processes as well as malignant epithelial cells resembling the cells of a catarrhal bronchitis.

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HEAT REGULATION IN DEMENTIA PRÆCOX

REACTIONS OF PATIENTS WITH DEMENTIA PRÆCOX TO COLD *

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THE responses of a homoeothermal organism to an extremely low environmental temperature and their adequacy in maintaining the body temperature at its normal level are measures of heat regulatory efficiency. A study of the reactions of schizophrenics exposed to extreme cold may reveal defects of ætiological importance. Experiments on heat regulation are particularly applicable for the discovery of any inadequacies in dementia præcox at the physiological level because the stimulus (cold) may be made sufficiently intense to tax the central thermogenetic apparatus to the utmost.

Lavoisier,[1] in 1777, observed that a man consumes more oxygen when the temperature of the air is 15° C. than he does when the environmental temperature is 32·5° C. Rubner,[2] among others, has demonstrated by calorimetric experiments that the heat production of the body is increased when there is a fall in the external temperature, the body temperature remaining constant. This phase of heat regulation was termed by Rubner 'chemical regulation' in contradistinction to 'physical regulation' which consists in an adjustment of the heat loss of the body when exposed to ordinary environmental temperature changes. Chemical regulation consists of a reflex increase in heat production in response to a very low external temperature when physical regulation or diminution of the heat loss no longer suffices to maintain the body near its constant temperature.

Variations from the normal in the oxygen consumption rate of schizophrenics have been reported by Hoskins.[3] However, the lower oxygen consumption rate under basal condition that he reported may be interpreted as being due to the inactivity of the schizophrenic or may be consequential to the disease, a factor which Hoskins did not omit in his interpretation. On

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the other hand, a study of changes in the rate of oxygen consumption induced reflexly by an intense stimulus of short duration and dependent upon the activity of the central nervous system and neuromuscular apparatus may reveal factors of ætiological significance. Moreover, patients with dementia præcox, who in their usual environment show only slight or no physiological variations from the normal, may react to extreme environmental changes in a manner indicative of a profound physiological disturbance.

METHOD

Fifty female patients diagnosed as cases of hebephrenic dementia præcox by the staff of the Elgin State Hospital were tested in the manner described below. They were all free from organic disease and were fairly cooperative with the procedure. Their median age was 30. Only 44 per cent. of the group were over 30 years of age and only five patients were over 43 years. The range was from 18 to 64. Their weights ranged from 83 to 193 lb., with 60 per cent. of the group weighing between 110 and 150 lb. The median weight was 121·5 lb. The duration of hospitalization was from 12 days to 15 years, with an average of two and a half years, 60 per cent. of the group having been in the hospital less than two years.

The oxygen consumption rate was determined for each patient under as nearly basal conditions as possible. The patients had had no food for 15 to 16 hours and rested from one to two hours before the tests were made. Fifteen or 20 minutes prior to immersion in cold water the oxygen consumption rate was determined on each patient. It was decided to immerse the patients in as cold water as possible. Four of the patients were tested in water at 58° F., one at 54° F. and one at 57° F. A temperature between 60° and 62° was finally found to be the most satisfactory and was used for 72 per cent. of the patients. Nine, or 18 per cent., of the patients did not cooperate in water at this temperature but did cooperate when the temperature was raised to 68° or 70° F.

At this point it is advisable to mention the fact that water has a greater heat conductivity than air and a considerably greater heat capacity. Heat from the body is lost much faster when exposed to cold water at a given temperature than in a medium of air at that temperature. Stated in another way, water at 90° F. feels cool, whereas air at that temperature feels very warm. Water at 60° F. is an extremely intense cold stimulus and is comparable with experiments in air at a much lower temperature. As soon as the patient was resting quietly in the water, the oxygen consumption rate was determined. The subject was then taken out, wrapped up in a warm blanket and put to bed. The total time spent in the water was usually from 15 to 20 minutes. Oral temperatures, pulse, complete blood counts and blood sugar determinations were taken in about 40 per cent. of the patients. No selections of patients were made for these additional observations. The

scope of the tests was merely enlarged as the work progressed. These determinations were made immediately after the oxygen consumption was tested in bed and in the water.

The recovery reactions of the patients were then tested and the above-mentioned observations were repeated after the patient had rested in bed, covered with blankets, 45 minutes to one hour after emergence from the cold water.

Twelve patients with chronic encephalitis and 26 healthy nonpsychotic subjects were subjected to the same procedures and served as controls. The patients with chronic encephalitis were tested twice within several weeks—once under treatment with atrophine and again after treatment had been discontinued for about a week. The control subjects included both men and women. A detailed analysis of the controls is given in papers to be published.[4,5]

RESULTS AND COMMENT

The reactions of the three groups are charted and tabulated. Fig. 1 shows that schizophrenics as a group differ from the normal control group in the rate of oxygen consumption when exposed to extreme cold. Fifty-six per cent. of patients with dementia præcox react to cold with an increase in oxygen consumption rate between 10 and 40 per cent., whereas 50 per cent. of nonpsychotic controls are grouped between 33 and 68 per cent. A histogram was not made from the results in chronic encephalitis because of the small number of subjects. However, a glance at Table V shows that the median change in oxygen consumption was similar in dementia præcox and in treated postencephalitic parkinsonism (21·00), and lower than the median in the nonpsychotic group (36·50). Table V also shows that the median temperature change on exposure to cold in the dementia præcox group was $-0{\cdot}8°$ F. as compared with a median change of $-0{\cdot}7°$ F. in chronic encephalitis (untreated), $-0{\cdot}6°$ F. (treated), and a change of $-0{\cdot}2°$ F. in the normals.

Reactions of the individual cases are given in Tables I to IV. Sixteen patients with dementia præcox, or 84·2 per cent. of the group in which temperatures were taken, lost from 0·2° F. to 3·0° F., with an average loss of 0·94° F. Only one patient showed a gain in temperature (0·2° F.). Two patients showed no change. Forty-four per cent. of the nonpsychotic subjects gained from 0·2° F. to 0·9° F., with an average of 0·3° F. Sixty-six per cent. lost from 0·2° F. to 1·2° F., with an average of 0·73° F. All of the untreated chronic encephalitics showed a decrease in temperature varying from 0·2° F. to 1·2° F., with an average of 0·73° F. The treated patients with chronic encephalitis had the lowest increase in oxygen consumption rate and showed the most marked decrease in temperature. A detailed comparison of the treated and untreated chronic encephalitics forms the subject-matter of another paper.[5]

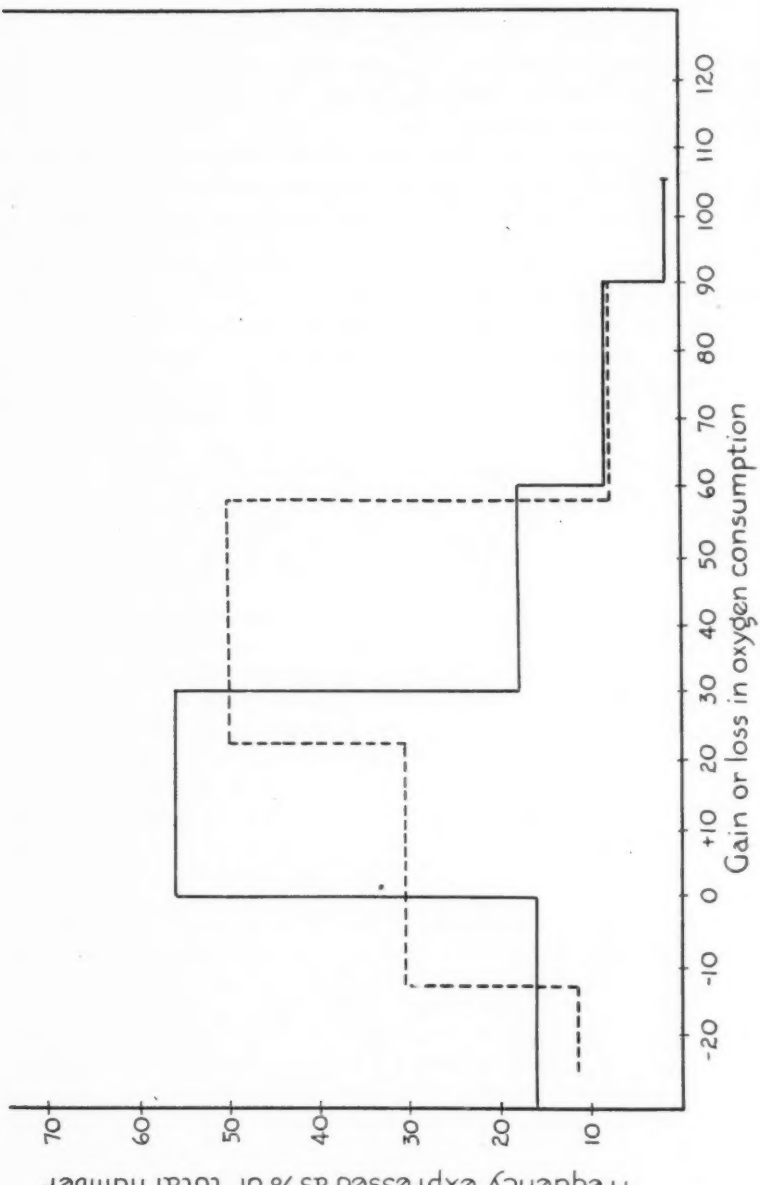

FIG. 1.—Histogram showing the gain or loss in oxygen consumption in 50 patients with hebephrenic dementia præcox as compared with 26 nonpsychotic healthy subjects, while placed for 15 to 20 minutes in cold water of about 60° F. The solid line represents the patients with hebephrenic dementia præcox. The broken line represents the nonpsychotic subjects.

The reactions of patients with dementia præcox, in general, resemble those of the chronic encephalities. They are of a lesser intensity than the responses of the nonpsychotic subjects, and are greater than the reactions of chronic encephalitics treated with atropine. It is evident, then, that schizophrenics as a group are defective in chemical heat regulation when compared with nonpsychotic subjects. Patients with dementia præcox have an inadequate response when exposed to cold. In only one of the schizophrenics

TABLE I. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Hebephrenic Dementia Præcox

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.D.	81	2	— 0·2	0	0·2
F.A.	63	—	— 0·4	—	—
F.R.	62	— 9	— 1·0	— 0·4	0·6
L.E.	53	0	— 1·0	— 0·2	0·8
R.R.	50	3	0·2	0·1	— 0·1
E.K.	48	—	— 0·8	—	—
H.S.	45	11	— 0·8	— 0·6	0·2
A.W.	39	— 35	— 0·6	— 1·3	— 0·7
I.W.	35	— 8	— 1·0	— 0·6	0·4
M.R.	28	0	— 1 5	— 1·2	0·3
F.Rh.	28	0	0	0	0
A.N.	22	—	— 0·8	—	—
V.B.	21	0	— 3·0	— 2·4	0·6
E.D.	17	0	0	—	—
E.W.	17	— 8	— 0·4	— 0·6	— 0·2
M.M.	16	—	— 1·4	—	—
D.H.	10	— 7	— 0·2	— 0·8	— 0·6
B.W.	7	14	— 1·0	— 2·8	— 1·8
B.S.	5	3	— 0·9	—	—

was there an overcompensation in heat production to cause a slight increase in temperature over the basal level (Table I). Eight of the 18 nonpsychotic subjects whose temperatures were taken in water showed an increase in temperature as a result of overcompensation in metabolic response to cold (Table II).

Our observations are in apparent contradiction to those recently reported by Cameron.[6] However, by employing an extremely low temperature we tested responses of increased heat production or chemical regulation, whereas Cameron exposing his patients to a temperature of about 20 degrees higher

than we used did not induce a reflex increase in metabolism. Physical heat regulation was studied by him and he concluded that although heat production in the schizophrenic reaction is low, the mechanisms of heat control are slightly more active in a schizophrenic than in a non-schizophrenic group. 'This overactivity was sufficient to compensate for the poor heat production even on exposure to cold.' One may, therefore, conclude from our observations that chemical regulation is defective in dementia præcox, and from

TABLE II. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Nonpsychotic Controls

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
M.B.	100	51	— 0·6	— 2·0	— 1·4
C.W.	67	9	—	—	—
F.K.	62	— 5	— 1·0	— 2·0	— 1·0
A.S.	57	41	0·2	— 0·4	— 0·6
L.A.	54	0	0·5	— 0·7	— 1·2
A.A.	50	7	— 0·3	— 0·3	0
H.S.	45	21	— 1·2	— 1·4	— 0·2
L.S.	37	32	— 1·1	— 1·0	0·1
M.W.	36	— 11	0·2	— 0·8	— 1·0
F.N.	33	1	0·6	— 0·2	— 0·8
T.W.	23	3	—	—	—
M.A.	21	—	— 1·1	—	—
I.F.	19	— 13	0·2	— 1·4	— 1·6
M.S.	14	8	0·6	— 0·2	— 0·8
M.B.	12	— 8	0·9	0	— 0·9
M.F.	10	—	— 1·0	—	—
M.Y.	5	— 4	— 0·6	— 0·6	0
W.S.	0	— 5	0·4	0·4	0
M.L.	— 15	—	— 0·2	—	—
W.H.	— 14	— 4	— 0·2	— 0·8	— 0·6

Cameron's observations that physical regulation is more active. The conclusion that physical regulation is more active in the schizophrenic reaction may be correct, but the fact that his patients were tested only two hours after a meal introduces another factor into the interpretation. Rubner,[2] in experiments on fasting and well-fed animals, has shown that food compensates for metabolism that is induced reflexly by cold. He has also criticized the results of Johansson [7] because the latter tested the reaction of his subjects only three hours after a meal. Moreover, Cameron himself has noted that the

heat response to the ingestion of food is more marked although less well sustained in the schizophrenic.

As mentioned above, we enlarged the scope of our investigation during its progress, adding, among other observations, temperatures during all test periods, and oxygen consumption rates 45 minutes to one hour after the bath. It so happened that the patients with dementia præcox on whom the additional observations were made fell in the group that had the higher range of oxygen consumption increase in cold water. Thus, a glance at Tables I and II reveals the fact that this smaller group of schizophrenics shows similar reactions to the nonpsychotic subjects in oxygen consumption gain or loss in cold water (col. 2). Nevertheless, these patients differ from the nonpsychotic controls in the reactions tabulated in the remaining columns of Tables I and II. Thus, none of the patients with dementia præcox showed a gain in oxygen consumption rate above 15, whereas four of the nonpsychotic subjects showed an increase (51, 41, 21 and 32 per cent.). The schizophrenics, then, did not maintain their increased metabolic response that they had on exposure to cold, whereas some of the normal subjects who had a similar metabolic reaction in cold water had a continued effect of the cold water 45 minutes to one hour later. The results tabulated in cols. 2 and 3 in Tables I and II further reveal the fact that the schizophrenics do not maintain the metabolic stimulation of the cold water. The patients with dementia præcox had a much greater drop in oxygen consumption rate after exposure from the high rate during exposure as compared with the normals.

The differences between the two groups are even more strikingly revealed in the last two cols. of Tables I and II. In these two columns are tabulated the gain or loss in temperature 45 minutes to one hour after exposure in cold water and the differences between the temperature readings during exposure and 45 minutes to one hour following exposure, respectively. Before we analyse these results we wish to mention briefly a physiological effect noticed after emergence from a cold bath and known as the 'after-effect.'[8, 9] After a person comes out of a cold bath and is wrapped up in a warm blanket it is found that his inner temperature is lower than it was in the bath. According to Liebermeister,[8] this lowering of the inner temperature depends obviously on the fact that the temperature of the peripheral part which became considerably cooled during exposure to cold tends to equalize itself with the inner temperature by means of the circulation. As a result of exposure to cold the superficial layer of the body is cooled to a considerable depth. After the subject is again exposed to a warm environment there occurs a reactive hyperæmia, the inner heat being conducted by means of the dilated blood vessels to the surface of the body. Thus, the inner temperature falls while the surface temperature rises until a normal gradient in the temperatures of the skin and the subcutaneous tissue is again set up.[10] If one studies the results given in the last column on Tables I and II, it becomes obvious that dementia præcox as a group does not have this reactive hyperæmia, as

shown by a failure of the inner temperature to fall. In fact, it is possible that a vasoconstriction occurs. Whereas seven out of 13 schizophrenics whose temperatures were taken showed a rise in temperature after the bath as compared with the temperature in the bath, only one of the normals (who also had hypertension) showed a slight rise (0·1° F.). The evidence adduced from the lack of a lowering of the inner temperature indicates that in dementia præcox there is no reactive hyperæmia observed in normal individuals, but instead there is a vasoconstriction. In this respect, also, the schizophrenics have reactions similar to the postencephalitics (Table III).

TABLE III. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Postencephalitics (Untreated)

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.B.	121	— 22	— 0·2	0	0·2
W.K.	85	— 1	— 0·9	— 0·3	0·6
H.H.	83	22	— 0·2	— 0·8	— 0·6
A.G.	49	35	— 0·2	0	0·2
F.P.	33	—	— 1·9	0·6	2·5
W.B.	29	7	— 0·7	— 0·6	0·1
R.F.	19	— 6	— 1·4	— 0·8	0·6
F.M.	17	— 4	— 0·4	— 0·6	— 0·2
C.C.	12	— 11	— 0·4	— 1·0	— 0·6
E.P.	— 18	—	—	—	—
T.H.	27	— 5	— 0·8	— 0·8	0
C.B.	— 46	— 43	— 0·7	— 1·1	— 0·4

Tables VI, VII, VIII and IX give the individual reactions of the patients as to pulse, respiration, leucocyte count and blood sugar. Table X is a statistical summary of the pulse and respiration in the three groups. There was no consistent reaction as to pulse in any of the groups. But a greater percentage of the schizophrenics reacted with an increase in pulse rate and the increase was greater than in the normals. There was a tendency towards a slight increase in respirations in all groups. Upon first entering the cold water the nonpsychotic subjects experienced a respiratory shock. This was not present in the schizophrenics, who breathed regularly and without effort from the very beginning. The observations on all subjects were made after the respiratory shock disappeared and breathing became regular. Loewy [11] observed this respiratory shock which soon disappeared and then the regular type of breathing was resumed. In 43 observations Loewy noted a lower

respiratory rate in 20, no change in 16, and a rise in seven on exposure to low temperatures. The respiratory frequency was lowered in a smaller number of patients in our experiments. There were insignificant differences in the respiratory changes in schizophrenia as compared with the control group.

The leucocyte count as a rule was increased on exposure to cold in all groups. An increase in the white blood count in cold baths was first reported by Thayer.[12]

There was no significant change in the blood sugar level on exposure in all groups. Swift, [13] who exposed 21 human subjects to cold air at 2° C. for

TABLE IV. THE EFFECT OF COLD ON OXYGEN CONSUMPTION AND ON BODY TEMPERATURE

Postencephalitics (Treated, Atropine Sulphate to Tolerance)

Patient	Oxygen consumption Gain or loss in cold water	Oxygen consumption Gain or loss 45 min. to 1 hr. after exposure in cold water	Temperature Gain or loss in cold water °F.	Temperature Gain or loss 45 min. to 1 hr. after exposure in cold water °F.	Difference between temperature readings during exposure and 45 min. to 1 hr. following exposure °F.
F.B.	74	—	— 1·0	—	—
W.K.	2	— 9	— 3·0	0	3·0
H.H.	16	—	— 0·1	—	—
A.G.	20	— 20	—	—	—
F.P.	22	9	— 1·4	— 0·4	1·0
W.B.	35	7	— 2·2	— 1·4	0·8
R.F.	29	7	— 2·2	— 1·2	1·0
F.M.	3	4	— 0·6	— 0·6	0
C.C.	27	8	— 0·4	— 1·2	— 0·8
E.P.	18	—	— 0·5	—	—
T.H.	38	— 14	— 0·6	— 0·2	0·4
C.B.	7	—	0·6	—	—

one hour and a quarter, found the blood sugar level unchanged and concluded that epinephrin secretion is not involved in the increased heat production. Grollman [14] concluded from his study on the effects of variations of the environmental temperature on various circulatory reactions in normal individuals that ' The quantity of blood thus diverted from the skin must be small and the absence of any increase in the total blood flow at low temperatures must be taken as evidence against the view that epinephrin plays the predominant part in producing the increased oxygen consumption observed at low temperatures.'

Thus, our observations corroborate those of Swift [13] and Grollman [14] and do not support the views of Cannon [15] and his pupils. Epinephrin, however, may play a predominant rôle in the defence against cold in the lower animals.

TABLE V. COMPARISON OF OXYGEN CONSUMPTION IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	50	−0·56	−0·50	−24 to 23	12	25·25	22·00	1 to 77	12	15·58	12·00	−9 to 60	26	−2·70	−1·50	−30 to 23
Gain or loss in tub of cold water	50	30·50	24·00	−14 to 115	12	34·25	28·00	−46 to 121	12	24·25	21·00	2 to 74	26	36·38	36·50	−14 to 114
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	15	−2·13	0	−35 to 14	10	−2·80	−4·50	−43 to 35	8	−1·0	5·50	−20 to 9	17	7·23	1·00	−13 to 51

COMPARISON OF TEMPERATURE °F.

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated; atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	20	98·40	98·40	97·40 to 99·20	11	98·20	98·40	97·30 to 99·00	11	98·20	98·40	97·60 to 98·80	19	98·10	98·00	97·40 to 99·00
Gain or loss in tub of cold water	19	−0·80	−0·80	−3·00 to 0·20	11	−0·70	−0·70	−0·20 to −1·90	11	−1·03	−0·60	−3·00 to 0·60	18	−0·20	−0·20	−1·20 to 0·09
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to water	13	−0·80	−0·60	−2·80 to 0·10	11	−0·50	−0·60	−1·10 to 0·60	7	−0·70	−0·60	−1·40 to 0	15	−0·80	−0·70	−2·00 to 0·40
Gain or loss from temperature in tub after 45 min. to 1 hr. rest in bed	13	−0·02	0·20	−1·80 to 0·80	11	0·20	0·10	−0·60 to 2·50	7	0·80	0·80	−0·80 to 3·00	15	−0·70	−0·80	−1·60 to 0·10

TABLE VI. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN HEBEPHRENIC DEMENTIA PRÆCOX

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.D.	10	4	— 1	1	11,000	9,400	10,100	69·82	68·92	66·66
F.A.	22	4	—	—	7,200	10,700	11,200	68·93	66·66	—
F.R.	8	1	1	— 1	6,800	7,800	7,800	72·72	71·43	66·66
L.E.	24	6	6	4	6,200	9,500	8,500	72·43	69·82	69·82
R.R.	15	2	1	0	8,400	11,200	8,400	80·00	78·50	78·04
E.K.	— 1	0	—	—	13,000	16,000	—	80·00	80·39	—
H.S.	— 2	3	—19	— 2	7,400	11,000	6,800	62·50	63·10	63·00
A.W.	— 3	4	— 3	0	9,000	11,000	12,400	74·07	74·07	73·52
I.W.	— 1	2	— 11	3	8,600	9,100	9,000	76·92	80·00	76·92
M.R.	— 7	3	— 3	0	6,200	5,600	7,000	76·59	77·22	76·92
F.Rh.	12	2	— 4	— 1	9,000	11,200	9,000	65·50	65·50	62·50
A.N.	4	3	—	—	—	—	—	—	—	—
V.B.	3	— 2	— 8	— 6	5,600	8,600	7,000	66·66	72·72	—
E.D.	— 6	0	—	— 1	8,000	10,800	8,100	64·51	74·07	66·66
E.W.	5	— 5	5	— 7	6,100	8,150	5,200	—	—	—
M.M.	4	2	—	—	—	—	—	—	—	—
D.H.	— 2	— 2	— 8	2	5,900	7,200	4,400	62·50	64·51	65·00
B.W.	— 3	2	— 9	2	5,000	9,600	8,800	71·43	69·40	—
B.S.	— 3	4	— 10	— 1	6,000	7,000	9,200	75·47	76·92	76·33

TABLE VII. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN NONPSYCHOTIC CONTROLS

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
M.B.	— 6	0	— 8	0	6,000	7,000	5,000	71·21	76·93	76·03
C.W.	— 3	1	9	1	6,000	13,800	7,300	68·91	71·43	71·43
F.K.	6	2	— 6	0	7,500	11,000	8,500	66·66	67·50	67·12
A.S.	0	2	— 8	2	6,600	7,000	7,200	76·92	76·33	76·33
L.A.	— 5	2	— 14	2	5,950	8,200	8,200	74·10	74·80	74·90
A.A.	5	0	— 11	1	7,800	12,000	5,600	66·61	68·90	68·70
H.S.	— 11	5	— 11	4	6,300	11,050	7,250	—	—	—
L.S.	4	1	8	1	5,000	9,200	7,500	81·30	85·83	81·30
M.W.	— 5	0	— 1	— 1	7,500	9,500	4,500	73·26	73·26	77·51
F.N.	— 2	0	— 11	1	6,200	8,000	7,800	81·30	66·60	—
T.W.	2	2	0	2	6,000	9,500	8,900	85·10	—	86·95
M.A.	4	0	—	—	9,000	10,000	11,000	82·98	85·10	—
I.F.	— 12	1	— 18	1	5,500	6,400	6,000	78·04	68·92	88·92
M.S.	— 4	2	— 2	4	6,700	6,600	5,000	74·60	—	74·00
M.B.	1	2	— 4	2	7,200	10,000	5,000	63·40	63·50	60·50
M.F.	— 6	3	—	—	9,100	9,300	—	69·65	68·92	71·43
M.Y.	— 9	1	3	1	5,000	6,800	6,500	81·30	75·18	83·33
W.S.	6	2	2	2	5,700	13,000	9,000	71·43	66·66	71·43
M.L.	— 5	— 3	—	— 4	—	—	—	—	—	—
M.H.	— 6	— 3	— 7	— 3	9,100	11,000	9,100	66·66	64·51	64·51

TABLE VIII. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN POSTENCEPHALITICS (TREATED)

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.B.	— 7	2	—	—	—	—	—	—	—	—
W.K.	3	1	6	0	10,500	11,500	6,400	67·12	67·50	68·92
H.H.	—	— 2	—	—	—	—	—	—	—	—
A.G.	7	2	— 7	— 8	11,000	17,000	10,500	80·00	83·33	83·33
F.P.	— 15	0	1	0	8,300	15,600	15,000	67·12	64·51	66·66
W.B.	— 4	0	— 8	— 1	6,800	7,300	7,600	72·10	70·66	72·10
R.F.	— 3	— 2	— 15	0	4,400	5,000	4,500	76·92	76·92	80·00
F.M.	— 4	— 1	— 6	— 2	6,600	7,000	6,200	83·33	83·33	90·90
C.C.	— 2	3	— 10	— 1	6,100	10,800	6,800	74·07	72·72	72·72
E.P.	— 7	— 1	—	—	—	—	—	—	—	—
T.H.	9	1	— 7	2	5,000	6,400	4,500	76·92	72·99	76·92
C.B.	17	2	—	—	6,200	9,000	7,100	67·12	66·66	62·50

TABLE IX. EFFECT OF EXPOSURE TO COLD ON PULSE, RESPIRATIONS, LEUCOCYTE COUNT AND BLOOD SUGAR IN POSTENCEPHALITICS (UNTREATED)

Patient	Pulse Gain or loss in tub of cold water	Respirations Gain or loss in tub of cold water	Pulse Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Respirations Gain or loss after 45 min. to 1 hr. rest in bed following exposure in cold water	Leucocyte Count			Blood Sugar		
					Before being placed in cold water	While in tub of cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water	Before being placed in tub of cold water	While in cold water for 10 min.	After rest in bed 45 min. to 1 hr. following exposure in cold water
F.B.	19	3	— 1	1	6,500	9,000	4,800	68·92	68·92	64·51
W.K.	6	4	6	1	7,750	9,300	8,200	85·10	66·90	—
H.H.	—	2	— 1	— 2	7,050	8,800	9,000	83·30	84·70	85·10
A.G.	18	7	0	0	6,000	8,900	7,200	71·43	65·62	74·04
F.P.	7	0	8	—	11,000	13,000	8,800	74·10	75·40	75·40
W.B.	— 8	3	— 7	— 1	6,000	9,100	10,000	86·90	88·80	90·90
R.F.	— 18	0	— 24	0	4,400	5,000	4,500	76·92	76·92	80·00
F.M.	— 5	1	— 8	1	6,500	7,700	5,400	100·00	95·20	100·00
C.C.	— 4	0	— 12	— 1	8,200	10,200	6,800	86·50	76·90	76·90
E.P.	—	7	—	—	—	—	—	—	—	—
T.H.	0	6	— 11	3	10,600	12,700	13,400	100·00	83·30	—
C.B.	— 7	— 1	— 15	— 2	10,000	13,750	9,100	80·00	76·90	80·00

TABLE X. COMPARISON OF PULSE IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated: atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	43	72·41	72·00	48 to 96	11	83·00	84·00	73 to 94	11	80·00	79	72 to 91	20	69·50	66·00	54 to 94
Gain or loss in tub of cold water	41	1·14	0	−16 to 24	10	0·80	−2·00	−18 to 19	11	0·54	−3	−15 to 17	20	−2·30	−3·50	−12 to 6
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	14	−4·50	−3·50	−19 to 6	11	−5·90	−7·00	−24 to 8	8	−5·75	−7	−15 to 6	17	−4·60	−6·00	−18 to 9

COMPARISON OF RESPIRATIONS IN

	Hebephrenic dementia præcox				Postencephalitis untreated				Postencephalitis treated: atropine sulphate to tolerance				Nonpsychotic healthy subjects			
	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range	No. subjects	Average	Median	Range
Under basal conditions	49	16·02	16	8 to 28	12	16·60	16·00	12 to 22	12	16·58	16·00	12 to 22	26	13·31	13·50	7 to 20
Gain or loss in tub of cold water	49	1·00	1	−7 to 11	12	2·66	2·50	−1 to 7	12	0·42	0·50	−2 to 3	26	1·65	1·50	−3 to 10
Gain or loss after 45 min. to 1 hr. rest in bed following exposure to cold	15	−0·50	0	−7 to 4	10	0	0	−2 to 3	8	−1·25	−0·50	−8 to 2	18	1·00	1·00	−4 to 4

Our findings do not indicate either an increased or diminished response in epinephrin in dementia præcox and do not support the conclusions of Freeman and Hoskins [16] that there is some adrenal deficiency in schizophrenia. However, these authors were eliciting the reactions of schizophrenics to a glycerin extract of adrenal cortex. Hartman, Brownell and Crosby [17] in experiments on rats concluded that the cortical hormone is concerned with heat production to maintain the body temperature.

In addition to observing that the schizophrenics, as a rule, did not have any respiratory shock on entering the cold bath, we observed that fewer of the patients with dementia præcox shivered than normals, and of those that shivered, the intensity of the shivering movements was considerably less than in the nonpsychotic subjects.

DISCUSSION

There is an agreement in the recent literature in ascribing to the hypothalamus the rôle of principal heat regulatory centre. From experiments on cats, Bazett, Alpers and Erb [18] concluded that the hypothalamus just cephalic to the corpora mamillaria was necessary for temperature control. This area included the nuclei surrounding the walls of the third ventricle and the infundibular nuclei. The patients with dementia præcox, considered as a group, on exposure to cold, did not respond with as intense heat production as the normals and had a greater drop in temperature. This inadequacy in heat regulation may be due to a disturbance in the physiology of the hypothalamus. The deficient response in shivering is further evidence that the disturbance is in the hypothalamus. Sherrington,[19] who observed dogs with a spinal transection, under extremes of temperature, noticed that when the animals were exposed to extreme cold there was an absence of shivering in the region innervated from behind the transection. Shivering occurred only headward of the spinal lesion. Shivering was concluded by Sherrington to be of central (diencephalic) origin. Keller and Hare [20] observed that animals in which the hypothalamus had been removed and the rest of the brain left intact could not be made to shiver and showed a release from control of the heat loss mechanism.

The failure of the schizophrenics to react with a vasodilatation when exposed to a warm environment is further evidence that the disturbance is in the hypothalamic nuclei. Davison [21] attributes the function of heat regulation to the nuclei tuberis proper and the mamillary bodies.

The reactions in dementia præcox resembled those elicited in post-encephalitic parkinsonism as a group. In view of the fact that the hypothalamus and the grey matter round the third ventricle are the seat of lesions in many cases of epidemic encephalitis,[22] the evidence for a physiological disturbance in that region in dementia præcox becomes more conclusive. One of us, however (Finkelman [23]), from a study of viscosity of muscles in catatonia and parkinsonian rigidity, has concluded that the

difference between the muscle tonus curves of chronic encephalitis and catatonia is evidence that the muscle rigidity in these two conditions is not due to physiological interruption at the same levels. This work does not invalidate our conclusions, as the cerebrospinal pathways that subserve muscle tonus are not involved in the experiments reported here. In other words, the hypothalamic centres to which we are attributing the physiological disturbance in dementia præcox as to defective heat regulation are probably not primarily involved in the mechanism of rigidity in catatonia.

The conclusion that there is a central disturbance in dementia præcox in the mechanism for heat regulation may be further strengthened if deficiencies in the peripheral mechanisms involving afferent and efferent pathways are eliminated. First we shall consider the afferent pathway. It is commonly held that in dementia præcox there is insensitivity to pain. Thus, one may prick the patient's tongue with a pin and notice that the tongue is not withdrawn. The conclusion that the pain is not felt is erroneous. Although the patient's outward demeanour does not betray his feeling of pain, there occur the usual respiratory changes with pain. What one observes is a poor defence reaction. The tongue is not withdrawn or it is withdrawn hesitatingly from the noxious stimulus. According to Huston,[24] there is no significant difference in the sensory threshold to direct current stimulation between a schizophrenic group and a comparable normal one. Temperature sensations are associated with reflex response to temperature. According to Ebbecke,[25] the sensation of cold depends on the difference established between the temperature of the cold end-organ in the skin and the layers surrounding it which are supplied with blood. A difference between the temperature of warm blood and a cooled skin around the cold end-organ will cause a sensation of cold. Even assuming a very slow blood flow, the temperature of the skin in our experiments was made so extremely cold (on exposure to 60° F.) as to set up a temperature gradient even with a slow blood flow. The threshold value was exceeded.

The next peripheral pathway to be considered and one which may be defective in dementia præcox is the efferent system. In a recent publication we have reported some observations on the reactions of patients with dementia præcox to dinitrophenol.[26] Schizophrenics react to dinitrophenol with as great an increase in oxygen consumption rate as that reported in the literature for nonpsychotic individuals. Dinitrophenol is a metabolic stimulant which acts peripherally. It is evident, then, that schizophrenics do not have a defective effector apparatus for metabolic activity. Spinal reflex pathways, including the afferent arc, a spinal centre and the efferent arc, are not physiologically interrupted in dementia præcox. In fact, Dorsey and Travis [27] reported experimental evidence of an increased activity of the lower neural level in catatonic stupor. In schizophrenics the reflex conduction rate (patellar reflex) was greatly increased over that of the normal subject.

There is one more possible localization of the deficiency in the mechanism for heat regulation, and that is the cortical component. Pinkston, Bard and Rioch, reporting observations made on dogs and cats which survived the removal of portions of the forebrain by six weeks to 28 months, could not decide ' whether or not there is a single centre in the brain responsible for the coordination of excitatory and efferent mechanisms ' (for heat regulation), but concluded that several levels of the nervous system, including the cortical, are necessary for normal temperature control. One might suppose that the disturbance in dementia præcox is in the association pathways that subserve heat regulation ; that there is a dissociation between the feeling of cold which is a cortical function and the motor innervation for increasing the metabolism. In other words, in dementia præcox there is an inadequate ' defence ' reaction to extreme cold. Man, through use of clothing and artificial heat, has become accustomed to a very narrow temperature range. The degree of cold to which we exposed our patients was a very uncomfortable, noxious stimulus, against which nonpsychotic individuals (not in the experimental situation) make an adequate defence. The schizophrenics as a rule stepped into the cold water unconcernedly. Bender and Schilder, reporting on unconditioned and conditioned reactions to pain in schizophrenia, state that it was characteristic of all the reactions (to pain) that the patients never actively attempted to escape or defend themselves. These authors conclude that the defence of the patient is no longer integrated. There is a dissociation between the appreciation of pain and the defence mechanism. We can similarly speak of a dissociation between the appreciation of cold and the defence mechanism. But since the ' defence mechanisms ' in heat regulation are involuntarily controlled reactions (shivering, vasomotor changes), the disturbance in heat regulation in dementia præcox is probably in the hypothalamus.

SUMMARY AND CONCLUSIONS

The reactions to extreme cold of a group of 50 patients with hebephrenic dementia præcox were observed. The oxygen consumption rates, temperature readings, blood sugar determinations and pulse, respirations, shivering, and other responses were noted before exposure, during exposure to water at 60° F. and during rest in bed after the bath. These reactions were compared with those observed in nonpsychotic subjects and in a group of chronic encephalitics exposed to the same experimental conditions. The patients with dementia præcox react to cold as a group with a lower heat production than the normals. The drop in temperature in the schizophrenics was greater than in the normals. Some of the nonpsychotic subjects maintain their metabolic stimulation for some time following exposure. This continued increased metabolic response was not found in schizophrenia. In the normal subjects there occurs a reactive hyperæmia, as evidenced by a drop in the inner temperature, after emerging from the cold bath into warm surroundings.

The inner temperature drops, the heat being conducted to the cooled body surface. This ' after-effect ' does not occur in dementia præcox as a group.

Schizophrenics do not have any respiratory shock on immersion in cold water, as a rule. This transient respiratory phenomenon was observed in most of the normal subjects. In schizophrenia there was an absence of, or a very slight shivering response. Many of the nonpsychotic subjects shivered, and some very intensely. There was no significant change in the blood sugar level in any of the groups, indicating that epinephrine, at least in human subjects, does not play a rôle as a calorigenic agent on exposure to cold. Many of the reactions were similar in schizophrenia and in post-encephalitic parkinsonism.

We can conclude that in dementia præcox there is a low heat production in response to cold. The heat production is not maintained after exposure and there is no reactive hyperæmia. Evidence is adduced that there is a physiological disturbance in the hypothalamus in schizophrenia.

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ÉTAT MARBRÉ

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The condition known as état marbré was first described fully by C. Vogt [24] in 1911 under the name of status marmoratus and has since been the subject of considerable interest and study. Nevertheless no full description has as yet appeared in any English journal, and therefore a brief introductory summary of the main clinical and pathological features may not come amiss.

On the clinical side, the condition usually manifests itself from earliest infancy, development is retarded and more or less severe mental defect is of constant appearance. The picture is one of double choreoathetosis, sometimes combined with epilepsy. Loss of emotional control is a prominent feature, and inability to use the muscles of expression and articulation sometimes occurs. In the majority of cases the condition remains stationary; in others severe generalized paralysis, often with torsion spasm and other contractures, eventually supervenes, and death occurs before or during early adult life. Pathologically the most striking feature is the peculiar marble-like appearance of certain areas of the striate body and to a lesser degree of other parts of the brain. The clinical picture, sometimes known as Vogt's disease, is considered by some to be sufficiently characteristic to be diagnosed during life, but, as we shall point out later, there are reasons for believing that the condition is not a clear-cut clinical or pathological entity.

Although uncommon, the condition is probably not so rare as might at first appear. It is probable that the majority of cases have failed to come under the care of competent neurologists; some may have been attributed to meningitis or encephalitis lethargica, while others have almost certainly been overlooked in institutions or elsewhere amongst a mass of heterogeneous cerebral palsies of childhood.

PERSONAL CASES

Case I.—D.L., a girl, age two and a half years, was admitted to the Fountain Hospital for mental defectives on August 13, 1920.

History.—Unfortunately the history of this case is very scanty, as there was no opportunity of interviewing the relatives personally and, since the patient's death, they have persistently ignored all letters. Except for some evidence of tuberculosis and paralysis on the paternal side, there is no family history of note. The patient was

* From the Central Pathological Laboratories of the London County Mental Hospitals.

the second of three siblings. No history regarding the periods of pregnancy, birth or early infancy is available.

State on Admission.—She was quite helpless and showed no signs of possessing any intelligence. She could not recognize nurses attending her, nor did she take any interest in her surroundings. Paresis of legs was noted.

Progress.—In March, 1924, she had her first epileptiform fit, and in the following month she contracted measles. In August, 1927, it was reported that she exhibited occasional coarse tremors, but had had no recent fits. Her habits were then clean, but she had to be hand-fed. A year later she was described as a case of spastic paraplegia with choreiform movements, faulty in habits and needing every attention. In January, 1931, her choreoathetotic movements were noted to be getting more severe, but she had had no fits for five years. In the following year, at the age of 13, she began to have frequent screaming attacks for no apparent reason. In June, 1932, she became more helpless and had to lie either in bed or in a special large 'basket,' as she could not sit up. Athetotic and choreic movements were much worse, although the screaming fits were less frequent. During these years she had made some intellectual progress and although she was never able to articulate, she understood what was said to her fairly well, liked to be 'made a fuss of,' smiled when her favourites approached her and could make affirmative and negative noises. Paralysis and wasting of her legs and left arm, and torsion-spasm of her trunk had been steadily progressing and were now extremely severe.

Clinical Condition in 1934 (æt. 16½).—Mental.—Her intelligence was too slight for tests to serve any useful purpose. She could not speak, but understood fairly well. She turned her eyes and tried to point in the direction of named nurses or patients in the ward. She took a considerable interest in her surroundings and became upset and emotional if she were not greeted by visitors to the ward. No screaming fits occurred, but she cried a good deal, often for no apparent reason. She was incontinent and altogether helpless.

Physical.—Her appearance was that of an emaciated girl of 12 years. Sexual development was slight, but some pubic and axillary hair was present. Menstruation never occurred. Her expression was strained and rather mask-like. Her smile dawned slowly and became wide and fixed and her facial appearance was characteristic of an extrapyramidal lesion.

Paralysis and Contractures.—There was extreme and generalized muscular wasting and weakness. Torsion contracture had reached a very severe degree; the thorax was grossly deformed, lateral curvature of the spine with convexity to the right being especially severe. The head was rotated to the left and the pelvis drawn upwards and to the left. Both legs showed adduction spasm, with the knees in contact and the feet widely separated. The arms also showed severe contractures, with flexion at the elbow joints, everted forearms and claw hands. Tendon reflexes were very brisk everywhere. On the left side there was an extensor plantar reflex; the right foot was too contracted for any plantar reflex to be elicited. The pupils reacted to light and on accommodation and the fundi were normal.

No fits or choreic movements had occurred recently and there was no evidence of myoclonus at any time since admission.

She gradually became weaker, terminal bronchitis and pulmonary congestion setting in a fortnight before her death (November 11, 1934).

PATHOLOGICAL EXAMINATION

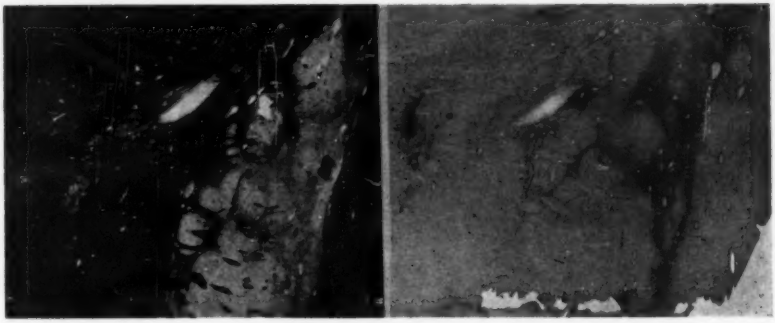
Lungs.—Signs of bronchitis and terminal basal congestion were present.

Heart.—The muscle was pale and flabby, the right ventricle somewhat dilated and the left ventricle hypertrophied. The valves were normal.

Liver.—There was considerable venous congestion and some degree of fibrosis round the bile ducts.

The pancreas and pituitary body showed more fibrous interstitial tissue than is usual and the spleen was congested ; otherwise these organs, and also the thyroid, suprarenals and kidneys were normal, both to naked eye and microscopical examination.

Brain.—Weight, 1,006 gm. *Macroscopical examination.*—The surface of the brain did not show any gross changes. Coronal sections revealed a symmetrical process in the striate body, involving both the caudate nucleus and the putamen. Both these nuclei contained whitish foci, which were connected with each other. The globus pallidus appeared to be intact. The reticulate zone of the substantia nigra showed a brownish discolouration, but no melanin pigment was detectable in the zona compacta. The hila of the



(*a*) (*b*)

FIG. 1.—' Marble state.' (*a*) Spielmeyer's myelin stain ; (*b*) Holzer's glia stain. × 7

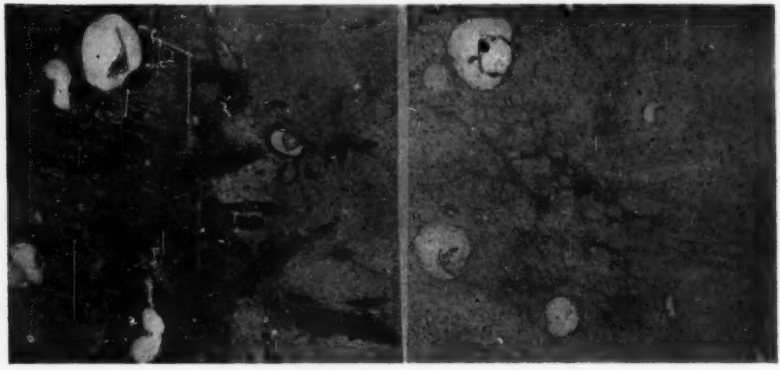
dentate nuclei of the cerebellum and the inferior olivary bodies were also of a brownish colour. The rest of the brain showed no noteworthy macroscopic changes.

Histological Findings.—Corpus striatum.—Myelin pictures of the striate body showed a symmetrical ' marble state ' in the dorsolateral parts of the putamen and the internal part of the caudate nucleus (fig. 1 *a*). In appearance and degree the marbling was somewhat similar to that of the fourth case of C. and O. Vogt.[23] Holzer's stain revealed that the hypermyelinized areas corresponded entirely with the glial scars (fig. 1 *b*), and there was unmistakable evidence that these scars completely covered the field taken by the hypermyelinized foci. In many parts of the affected areas the ganglion-cells had disappeared. In Nissl sections the glial proliferation was not sufficiently well marked to give any idea of the intensity of the process. The glial fibrous scarring was very dense, the individual fibres being rather delicate. The vessels showed fibrotic proliferation of the walls, but neither

here nor elsewhere were there any signs of recent activity of the process. The myelin-fibres of the scars intertwined very densely. The hypermyelinized fibres were usually delicate and showed frequent thickenings and end-bulbs, but no loops.

Several points of special interest arise from the examination of these sections. First, the external capsule was seen to be changed into a strip of dense glial fibrosis, the scars of the ' marble state ' often constituting only a ramification of this more massive scar (fig. 1 *b*). The scar in the external capsule extended irregularly and to a lesser degree into the claustrum and capsula extrema. Less frequently a similar picture was evident at the margin between the external capsule and the caudate nucleus.

Secondly, the large striopallidal fibres were not involved and could be



(*a*) (*b*)

FIG. 2.—Network-like glial scars at the junction of putamen and globus pallidus. (*a*) Spielmeyer's myelin stain ; (*b*) Holzer's stain. × 20.

seen, often in large numbers, lying intact within the scar tissue. The ansa lenticularis, as well as the lamellæ of the globus pallidus, was sclerosed. The scarring of the external lamella was in some places connected with the ' marbled ' scars of the putamen. At the junction of the putamen and the globus pallidus, network-like ramifications of glial scars could frequently be observed (fig. 2). This retiform structure was brought about by the glial scar tissue expanding round the transversely or obliquely cut large striopallidal bundles, which again were spared. This network had a superficial resemblance to the état marbré, but it was of much smaller size and was not hypermyelinized.

In the dorsal parts of the globus pallidus were scattered patches of demyelinization with corresponding gliosis, frequently showing a perivascular distribution. The ganglion-cells did not show any remarkable changes, but some of the macroglia cells were hypertrophied, although they never reached

the size of the Alzheimer type of cell. No increase of pigment could be detected with Nissl, fat or iron stain, nor were there any ' pseudo-calcium ' deposits either within or outside the vessel walls.

Thalamus and Hypothalamic Regions.—There was a marked subependymal glial sclerosis at the surface of the thalamus, with particular accentuation in the region of the terminal vein. The corpus Luysii was only slightly decreased in size and Forel's field was sclerosed.

Substantia nigra.—In both the compact and reticulate zones of the substantia nigra a well-marked glial sclerosis was seen. In the reticulate zone Nissl's stain revealed a definite increase in the greenish, bluish and brownish

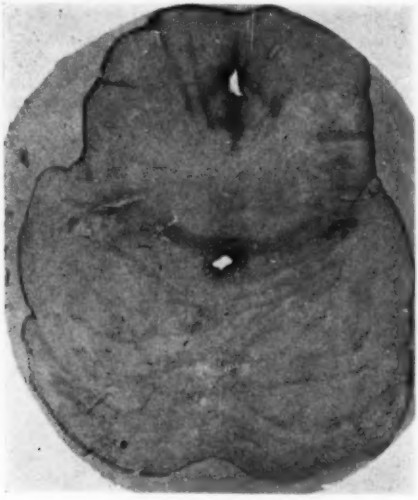
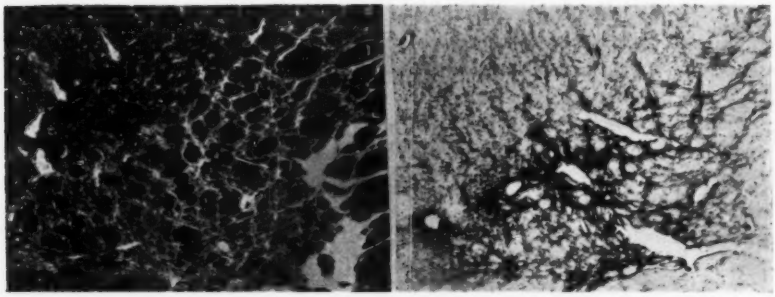


FIG. 3.—Pons. Holzer's glia stain. × 3.

pigment described by Hallervorden and Spatz.[26] It was situated in the glial and compound granular cells and as free-lying globules, particularly near the vessels. It gave only a partial iron reaction (after being fixed in formalin for a long period) and rarely stained with Scharlach R. The amount of pigment although considerable fell far short of that of the original case of Hallervorden and Spatz. In the compact zone melanin was entirely absent from the ganglion cells, although the cells themselves were still present. With reference to Helfand's [25] recent findings in état dysmyelinisé, it may be mentioned that melanin was present in normal quantity and quality in the locus cœruleus and dorsal nucleus of the vagus nerve.

Midbrain.—Around the aqueduct and the foramen cæcum there was a fairly heavy gliosis (fig. 3). From the foramen cæcum it extended symmetrically on both sides in a wing-like manner just below the mesial fillets. In

the lateral part of this scar there was again a network arrangement round the transversely cut, well-preserved myelin bundles (fig. 4). Within the brachia



(*a*) (*b*)

FIG. 4.—Pons, dorsolateral part of the pes, showing glial scars round preserved fibre bundles. (*a*) Spielmeyer's myelin stain ; (*b*) Holzer's stain. × 18.

conjunctiva the tendency to decolourize the myelin dye was abnormally great, although neither definite demyelinization nor glial sclerosis was found.

Medulla oblongata.—The floor of the fourth ventricle and the hila of both the olivary bodies showed considerable gliosis. There was no dropping out of the ganglion cells, but they showed, as they frequently do, increased deposits of lipofuscin.

Cerebellum.—The hilum of the dentate nucleus was almost completely

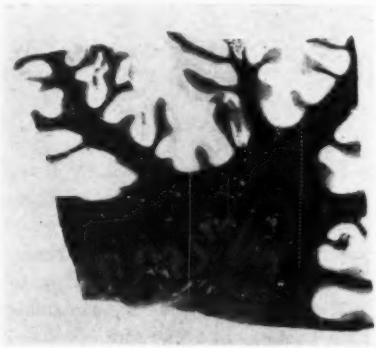


FIG. 5.—Demyelinization in the region of the dentate nucleus. Spielmeyer's myelin stain. × 3.

demyelinized (fig. 5), and showed corresponding glial proliferation, although the strands of ganglion-cells appeared to be well preserved. In the rest of the cerebellar white matter there was also a delicate fibrous glial prolifera-

tion, associated with a slight and sometimes patchy reduction in staining power of the myelin sheaths. Sections of the axis-cylinders did not reveal any marked change.

Cerebral White Matter.—The same diffuse or patchy inability to take up the hæmatoxylin of the myelin stains was observed in widespread areas of the cerebral white matter, frequently associated with a slight glial proliferation. Particularly well marked was the demyelinization of the white matter in the occipital lobe, with preservation of the arcuate fibres. Throughout the cerebral and cerebellar cortex no noteworthy changes occurred except for a diffuse subpial gliosis.

Case II.—M.E.R., a woman, aged 42 years, was admitted to Leavesden Menta Hospital on January 29, 1932. This case will be clinically and pathologically described

FIG. 6.—Etat marbré of the thalamus. Spielmeyer's myelin stain. × 2½.

in full in a further paper, but certain features must be mentioned here, because of their important bearing on our present subject. Most remarkable of all was the appearance of a network of hypermyelinized glial scars in the medial nucleus of the thalamus (fig. 6), although there was no actual 'marble state' of the corpus striatum. In addition to this there were several points of resemblance to our first case, including a sclerosis of the external capsule and ansa lenticularis, an increase of pigment in the globus pallidus and reticulate zone of the substantia nigra (which also showed a heavy sclerosis), general subependymal sclerosis, demyelinization of the hilum of the dentate nucleus and, in a patchy manner, of the cerebellar white matter, sclerosis of the hila of the olivary bodies and, finally, a diminution in the capacity of the cerebral white matter to take up stain.

Clinically the patient suffered from mental defect and cerebral diplegia from earliest infancy. She was able to walk at the age of five years, but became paralysed during adolescence and died at the age of 44 years in a state of idiocy and generalized spasticity.

DISCUSSION

The pathological findings in our first case leave no room for doubt as to its identity with those previously described as état marbré. Apart from the glial scars, it was possible to demonstrate foci of hypermyelinization, typically distributed, in the putamen and caudate nucleus. Moreover, in contradistinction to the findings of Case,[4] the hypermyelinized foci and the glial scars could be shown to occupy identical areas. In this connexion it may be mentioned that the ' marbling ' is not visible with the same intensity in every section or even in neighbouring sections, which may account for the difficulty in demonstrating the identity of the sites of marbling in glial and myelin pictures in some cases.

Both in Case I of this paper and in A. Meyer's [12] previous case there was a considerable sclerosis of the external capsule, extending to a lesser degree towards the region of the claustrum and the capsula extrema. This scar was present also in other published cases, e.g. those of Bielschowsky,[2] and Loewenberg and Malamud.[11] In some places, particularly in the caudal parts of the putamen of our case, this external capsule scar was very heavy and the état marbré appeared to be merely a ramification of it (fig. 1*b*). A somewhat similar condition occasionally could be seen at the junction of the internal capsule with the caudate nucleus. It is true that in our cases, as well as in those previously published, ' marble ' scars were seen which had no connexion with the scars in the adjacent white matter. Such occurrences call to mind the socalled putamen-claustrum type of large hæmorrhage, seen for the most part in hypertensive conditions.

How wrong it is to speak of état marbré as a striate system disease is shown by the widespread incidence of the lesions. They are to be found in globus pallidus (particularly in its efferent tracts, the lamellæ and ansa lenticularis), in the substantia nigra, where compact and reticulate zones are equally affected, in all subependymal regions of the ventricular system, in the dentate nucleus, in the olivary bodies, in the white matter of the cerebellum and to some extent in that of the cerebrum. Wherever one sees changes, they are qualitatively identical with those underlying the marble-formation—that is to say, more or less circumscribed glial scars often perivascularly arranged and with no signs of recent disintegration of tissue.

Hypermyelinized scars in the thalamus have been described with increasing frequency during recent years (A. Meyer,[12] Gozzano,[7] Loewenberg and Malamud,[11] R. Holzer [10]), and our second case adds a fresh contribution, as, in addition to this, it is distinguished by the absence of a striatal ' marble state '. Etat marbré has also been found in the claustrum by Myslevecek.[13] The sclerosis in the olivary body is of special interest because of a similar finding in van Bogaert's case,[3] but in contrast with the latter no myoclonic twitchings were observed during life in ours.

The affection of the substantia nigra, associated with a considerable increase of Hallervorden-Spatz pigment in the reticulate zone, and also that

of the dentate nucleus brings into discussion the possible relationship of état marbré with certain other conditions, particularly Hallervorden-Spatz disease (état dysmyélinisé) and the affection of the dentate-rubral system, observed in a case of athetosis by Bostroem and Spatz. A combination of état marbré and état dysmyélinisé has been recorded a few years ago by Onari,[14] but what this coincidence means pathogenically and how often it occurs has not yet been satisfactorily explained—the less so, as the nosological interpretation of the changes in état dysmyélinisé becomes more and more complicated (Helfand [25]). We shall refer to the whole problem in a subsequent paper, dealing with état dysmyélinisé. The complexity and extent of the lesions in cases such as ours not only emphasize the difficulties of localization of clinical signs, such as athetosis, etc., but should make us very chary of regarding état marbré (' Vogt's disease ') as a unity, which can be diagnosed during life. A similar conclusion must be reached after considering the various theories propounded to explain the causation of état marbré. It seems to us that the nosological conceptions of this condition are based on far too few thoroughly examined cases, and might undergo considerable alteration with increasing experience.

PATHOGENESIS

The original view of C. and O. Vogt,[23] that état marbré is a malformation, has been abandoned by the great majority of writers (W. Scholz,[18] Schwartz,[19] A. Meyer,[12] Myslevecek,[13] Loewenberg and Malamud,[11] R. Holzer,[10] etc.). An inflammatory origin was favoured by some workers (Bielschowsky,[2] Loewenberg and Malamud,[11] Case 4), and trauma preceded one of the cases of Scholz.[18] A constitutional factor has been suggested by cases of Anton, Oppenheim and C. Vogt, Scholz,[18] Bielschowsky [2] and van Bogaert.[3] Van Bogaert's case, however, was complicated by the presence of Unverricht-Lundborg disease. Schwartz [19] was the first to suggest birth trauma as its cause, and this view has been strongly supported by several authors (Pfeiffer,[16] Lotmar,[27] etc.).

A review of the literature reveals, as far as we can discover, only 23 cases of état marbré which have been pathologically verified. In seven of these no birth history was given, and of the remaining 16 as many as nine showed definite signs of birth trauma. Among the positive cases we have included the first case of Loewenberg and Malamud and that of Case, although the authors themselves do not appear to attach any importance to the evidence of birth lesion. Nevertheless, impartial consideration of the history of both these cases makes it impossible not to consider birth trauma as a factor. The same applies to the previous case of A. Meyer, in which a review of the history leaves no room for doubt that a definite birth injury occurred. The perivascular gliosis and endarteritis in this case, originally considered to be the result of an inflammatory process, can easily be interpreted as the result of anoxæmia (Pentschew [15]), and it needs no further discussion to be assured

that the evidence in favour of an inflammatory process, in other socalled inflammatory cases, is based on similar histological findings. At this point we must make it clear that we do not accept evidence of birth trauma too easily. There must be a history of difficult or asphyxiate delivery followed by fits or other neurological symptoms in early infancy. Less serious disturbances are discounted. Our collection of cases from the literature shows, furthermore, that cerebral lesions were thought to have been present from birth in 13 cases, whilst in a further seven cases there were apparently definite signs of the disease within the first year of life, although athetosis may have developed later in a few of them. The whole of this evidence strongly suggests that in the great majority of cases état marbré originates in prenatal, natal or very early postnatal life.

The figures given above are of interest in that they suggest that birth trauma, although it may admittedly not cover all cases, is an important ætiological factor in a considerable number of them. Perhaps it would be more relevant and more useful to look not for a uniform cause of état marbré, but for a uniform pathophysiological mechanism which might be common to several ætiologically different conditions. Such a view is the more attractive as it has been successfully applied to the related question of plaques fibromyéliniques. It has been shown by Spatz [20] and his co-workers that plaques fibromyéliniques are brought about by such different diseases as CO poisoning, arteriosclerosis, hypertension, etc. A similar state of affairs may well apply to état marbré, which may turn out to be a pathological state of multiple ætiology. As regards its mechanism, two problems are of particular interest : that of the hypermyelinization of the scars, and that of their retiform arrangement and special localizatory predilection.

As regards the hypermyelinization, it has been made sufficiently clear by Spatz, Mittelbach, Pentschew and others, that small glial scars of elongated shape and vascular origin are essential to its production, but there is no unanimity of opinion as to the details of pathogenesis. The majority of writers hold the view that the excess of fibres has been brought about by regeneration. Bielschowsky [2] has, however, suggested the idea of a production of myelin around originally naked axis-cylinders. His explanation is interesting in the light of our newly acquired knowledge of the myelogenetic function of glia. The excess of myelin would be, so to speak, a by-product of the pathological hyperactivity of the glia. The difficulties of interpretation of the histological picture are so great as to render exact histological proof of one or the other of these theories almost impossible.

It is equally difficult to account for the peculiar retiform arrangement of the scars and their predilective site. Although glial scars of a perivascular and patchy type are scattered over many regions of the brain, typical état marbré seems to occur most frequently in the striate body and in the cortex, and only rarely in the thalamus and other regions. Accordingly C. and O. Vogt suggested a ' pathoclitic ' disposition of the striate body and the cortex.

One must be aware, however, that this is more in the nature of a statement, useful though it may be, than an explanation of the problem, upon which only comprehensive comparative studies can hope to throw more light. In this effort Schwartz has led the way by relating état marbré to the lesions seen after birth trauma, but so far his histological evidence is superficial. Further systematic research on normal and pathological conditions of the newborn should be of value and might enable us to see early stages of état marbré. Although état marbré is almost exclusively a condition of the early epochs of life, it should also be looked for in vascular lesions of later years. There it might occur, as we find with plaques fibromyéliniques, in the form which Hallervorden [8] has called the 'paradoxical appearance of status marmoratus without myelinization.' On this point only few and by no means convincing observations, notably by Gozzano [7] and Stief,[22] are as yet available. Berlucchi's [1] recent description of structures simulating état marbré in the striate body of normal brains should be clearly distinguished from the definitely pathological hypermyelinized scar, here under discussion.

It might even be necessary to go back to more fundamental studies of the peculiarities of the blood supply in the regions affected. In this regard Schwartz's conception of the terminal vein determining localization in birth trauma has not been sufficiently utilized. As a further example we can take K. Stern's [21] recent study of the extension of vascular lesions in the pons. His explanation of retiform lesions brings his paper particularly into discussion here. According to him, physical factors, as, for example, the degree of pressure of hæmorrhages and the differences in consistency of the tissue, are more important in determining the extension of lesions than is generally realized. The retiform structures studied by him have been brought about by a tendency for the large pontocerebellar fibres to be spared. We should do well to remember, however, that the resemblance between Stern's pictures and those of état marbré is only superficial. The état marbré differs not only in size, but also in the lack of spatial relationship between the preserved striopallidal bundles and the scars. On the other hand, retiform structures, comparable to those described by Stern, have been found in the putamen (outside the état marbré) and pons of our first case (figs. 2 and 4). Further research may prove whether we are dealing with more than a merely negligible similarity.

SUMMARY

1. Two personal cases are described, one of which showed an état marbré in the striate body, the other in the thalamus alone. Both cases were the subjects of severe mental defect and quadriplegia from infancy. The first patient suffered also from torsion spasm, generalized fits, athetosis and other involuntary movements and screaming attacks.

2. With the état marbré were associated lesions in the globus pallidus, black and red zone of the substantia nigra, subependymal regions, dentate

nuclei and olivary body. The cortex was unaffected ; the myelin sheaths of the white matter showed some slight diffuse or circumscribed lack of staining power.

3. The conception of état marbré as a nosological entity is criticized. Particular stress is laid on the importance of birth trauma in many cases, and further investigation in this field is urged. The pathogenesis of retiform lesions is discussed with reference to recent investigations.

We gratefully acknowledge our thanks to Dr. R. Mackenzie Stewart for furnishing us with the pathological material and clinical information of our second case, and to Mrs. A. Meyer for the preparation of the histological sections and microphotographs. Our thanks are also due to Dr. James Nicoll, Medical Superintendent of the Fountain Hospital, for permission to publish the first case, to Dr. F. Golla, Director of the Central Pathological Laboratories of the London County Mental Hospitals, for his kindly interest and to the Rockefeller Foundation for a grant to one of us (A. M.).

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SOME OBSERVATIONS ON MASKED EPILEPSY AND THE SIMULATION OF TRAUMATIC EPILEPSY BY CEREBRAL TUMOUR, WITH SPECIAL REFERENCE TO HEAD INJURIES WITHOUT FRACTURE *

By

LEWIS R. YEALLAND, London

In an analysis of 500 cases of head injury without fracture, epilepsy was discovered for the first time after the accident in 17 of them. But, in each case, cerebral tumour was either proved to be present or else strongly suggested clinically. So far as it was possible to judge by the history of the accident in the various cases, the injuries seemed to be of a trivial nature. The investigation, therefore, resolved itself into an attempt to ascertain, if possible, the relationship between head injuries without fracture and epilepsy in cases of cerebral tumour. The cases fell under the following clinical classification: (1) Those in which epilepsy was the predominating feature, and referred to here as traumatic epilepsy simulated by cerebral tumour; (2) those in which epilepsy was more or less obscured by the subjective symptoms common to traumatic neurosis, and referred to here as masked epilepsy.

I. TRAUMATIC EPILEPSY SIMULATED BY CEREBRAL TUMOUR

There was some evidence to indicate that a protective mechanism exists between a tumour and the brain, which may be either permanently or temporarily damaged after a head injury without fracture. The persistence of epilepsy on the one hand and its gradual subsidence on the other after a head injury were taken as evidence of the progress occurring in the traumatic breach. Illustrations representing each type will be given.

Epilepsy Persisting.—A timber porter, age 45, when standing, was struck in the right postparietal region by a 12-lb. wooden plank which fell flat from a distance of 10 feet. He was momentarily dazed, but after an hour continued his work. The following morning he had, for the first time, an epileptic fit and complained of headache. The fits increased in frequency, and he was sent to hospital, a week after the accident, as a case of traumatic epilepsy. On admission there were double papilloedema (1·5 D), right pyramidal signs without much weakness, and slight motor aphasia. The cerebrospinal fluid contained 0·3 per cent. protein, and globulin in excess. During the first fortnight the fits (right Jacksonian) increased in frequency and at the end of

* Read at the Second International Neurological Congress, London, 1935.

that time he became totally hemiplegic and aphasic. Mr. Dickson Wright exposed a growth situated in Broca's area which at autopsy was found to be a carcinoma surrounded by hæmatoma. Previous to the accident the patient was apparently in good health.

Epilepsy Subsiding.—A labourer, age 24, was kicked on the forehead when playing football. He struggled to his feet and continued the game. The following day he had, for the first time, an epileptic fit. For 10 years he attended a London hospital for epilepsy and was relieved by luminal. He had been free from attacks for two years when, at the age of 36, he fell down a manhole, not in a fit (according to an eye-witness). He got to the surface almost at once and continued his work. The following day he had a seizure, and thereafter several attacks each day for a month when he was sent as a case of traumatic epilepsy by a firm of solicitors. He was admitted to hospital. According to the history the fits had often begun in his left hand, immediately after which he became unconscious. The fits observed in hospital were generalized. A physical examination disclosed double papillœdema (R. 3D; L. 4D); left hemiplegia (weak left face, left extensor response, without apparent paralysis). The cerebrospinal fluid contained nothing pathological. A cystic glioma attached to the pia over the right motor arm area was exposed and 10 c.cm. of yellowish fluid were removed by Mr. Wakeley. Dr. Carnegie Dickson reported a section of the growth as an astrocytoma.

II. MASKED EPILEPSY

Epilepsy was masked in 12 cases. Among the circumstances, apart from the subjective symptoms common to trauma, which tended to obscure the recognition of corticomotor and corticosensory fits were: (*a*) Complete amnesia of the somatic experience; (*b*) difficulty in describing a cortical experience, especially when it was sensory; and (*c*) the sudden onset of hemiplegia.

(*a*) *Complete Amnesia of the Somatic Experience.*—Unlike experimental epilepsy, the epileptic phenomenon observed clinically is, as a rule, composed of two elements, viz. psychological and somatic. The psychological element in some of my cases was so prominent a feature of the attack as to obscure completely all recollection of the somatic element. In spite of a careful search for evidence of cortical experiences in those who suffered from periodic attacks of disturbances of consciousness, the difficulties in detecting epilepsy were greater in the case of non-convulsive fits. Such terms employed by the patients as 'collapse,' 'stroke,' 'faints' and 'giddiness' sometimes led to the disclosure of epilepsy. If the case about to be described had been sensory instead of motor, it would have been impossible to interpret the significance of the term 'giddiness.'

A gardener, age 24, was sent for recurring attacks of giddiness which followed a blow on his forehead caused by the swinging of an iron gate. Giddiness, which occurred in the morning, had continued for a period of one month. He gave a history of two severe attacks of headache unaccompanied by vomiting. His appearance was heavy but otherwise healthy. Although intelligent in answering other questions, he was unable to provide any further information on the nature of the giddiness than: 'I just come over giddy.' He had no idea of its duration but thought the 'turn' lasted a 'short time.' A physical examination revealed no signs of organic disease. The optic discs were normal. When the examination was finished he was asked to

dress, but instead of doing so, he remained lying on the couch, and there occurred a typical left Jacksonian fit which began in the arm and spread to the face and leg simultaneously. The left plantar was extensor and remained so for about five minutes. When, after he had dressed, he was asked to relate what had happened, it was impossible to elicit anything more from him than, 'I just came over giddy.' No recollection of having been convulsed was retained. A week later he was admitted to hospital. A physical examination revealed nothing abnormal. Renal efficiency tests were normal and the Wassermann reaction was negative. The cerebrospinal fluid contained 0·06 per cent. protein, and globulins were present. There was no increase in cells. After two months' rest in bed the symptoms subsided. He has been under observation for three years and the left plantar reflex has been extensor for the last three months.

(*b*) *Difficulty in Describing Corticosensory Experiences.*—In four cases the somatic experience was but vaguely retained and could only be symbolized

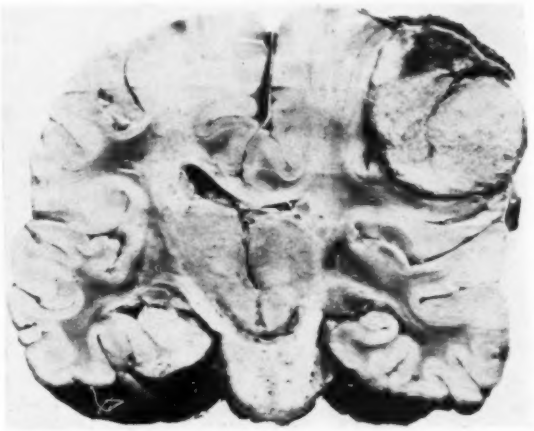

FIG. 1.

in a language the clinical interpretation of which presented difficulties. Thus, in addition to prolonged observation, a grim and laborious coaxing was necessary in leading the patients to symbolize their sensory experiences in language which admitted of clinical interpretation. In others the somatic element was recalled in a clean-cut and well-defined description.

A tailor, age 52, was sent because he was 'nervy and giddy' after striking his head against a mantelpiece. An examination revealed kinæsthetic signs in the left hand (compass test 4 cm.). No other evidence of organic disease could be detected. There was no papilloedema. He was persistent in his refusal to admit having difficulty in using his left hand, and he denied having headache. During the same week he was admitted to hospital and in a few days' time said he had recovered and wanted to return home. After a lengthy interrogation relating to his left side, he admitted this much, that his left hand sometimes went 'twiddley,' and sometimes, 'it goes funny all down that side.' After being persistently urged he ultimately symbolized the sensations

in his head, not as headache, but scornfully by the description : ' Them ain't headache, them is hell ' ; and thereafter persistently denied that he suffered from headache. The cerebrospinal fluid showed 0·1 per cent. total protein, and an excess of globulin ; no other pathological changes were noted. The following week Mr. Wakeley exposed the meningioma shown in fig. 1.

A tram driver, age 60, as the result of a mechanical defect in the magnetic brake control of the tram he was driving, collided with a stationary tram in front. He was thrown backwards against the window at the rear of the driving cabin, his head striking the glass without breaking the latter. He felt dazed but did not lose consciousness, and when the necessary brake adjustments were completed he was able

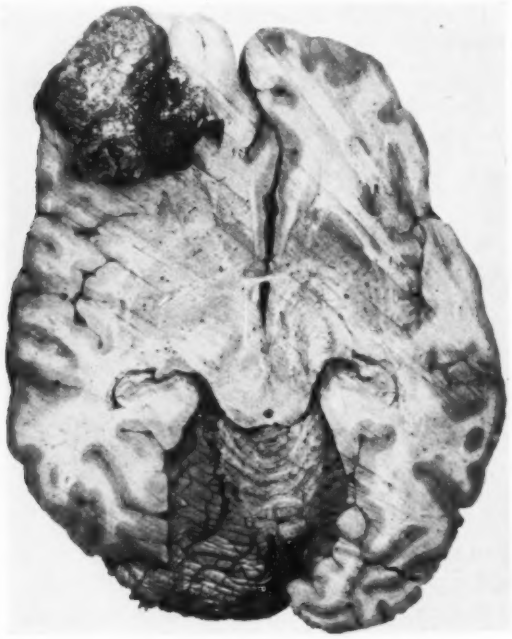

FIG. 2.

to continue driving. The following day he began to lose confidence in himself because of giddiness. A week after the accident headache and pain behind the eyes were noticed for the first time and he was obliged to stop work. A month after the accident he was sent to hospital, where a physical examination disclosed no signs of organic disease. He appeared to be mentally retarded and was admitted for observation. The cerebrospinal fluid showed three cells, 0·06 per cent. total protein, and excess of globulin. During his first week in hospital he was observed to be drowsy on some occasions. A month after his admission he complained of unpleasant smells in the ward which lasted from 15 minutes to an hour. He was unable to give any information as to their nature. Three months after his admission papillœdema appeared in the right eye and within a fortnight the left eye was similarly affected. He complained

of 'numb feelings,' but, although he said they were present on one side only, he differed from time to time as to which side was affected. Papillœdema increased to 5D. Mr. Tanner performed a left subtemporal decompression; the brain was found to be under great tension.

The following case illustrates the unmasking of an uncinate fit, perhaps by the added impressions consequent upon new experiences.

In brief, a woman, age 56, was stunned by a toss from her horse. She finished the day's hunt. The following day she felt 'headachy, nervy, and a sort of burny feeling in my nose.' Not having quite recovered her former health after six months, she made Africa her destination for a complete change. While she was there she 'kept on smelling a sort of smell like burning natives,' and since her return to England this sensation has periodically recurred. She was vague about its duration and frequency. Sometimes she said 'I have numbness in my hand or leg.' When asked which side she replied 'What difference does it make, it lasts such a short time.' But when she referred to the numbness, she invariably looked at the palm of her left hand, which she stroked with her left thumb. A diagnosis of tumour has not yet been substantiated in this case.

A school teacher, age 45, was admitted to hospital after slipping on the floor and striking the back of her head. On examination no physical signs were detected. She had headache and sickness in the morning. When questioned as to her sensory experiences she disclosed the fact that periodically there was a sudden appearance of 'white nuns or groups of nurses dressed in white' to the left of her bed. When further questioned she said that if she believed in ghosts she would think they were ghosts. The patient was not decompressed but the brain at autopsy was found to contain the tumour with hæmorrhage as shown in fig. 2.

(*c*) *The Sudden Onset of Hemiplegia.*—Difficulty was sometimes experienced in discovering the sequence of events centring round an accident. Mental phenomena following in the wake of trauma in general were sometimes of such a nature as to produce a degree of introspection. Thus, symptoms hitherto indefinite or disregarded by the patient may have become a prominent source of worry. Preexisting disease was, therefore, sometimes in a double sense discovered by accident, and the ætiological relationship between the head injury and the epilepsy was for a time left in doubt.

The sudden onset of hemiplegia with unconsciousness or a state of coma lasting hours or days masked the existence of epilepsy in six cases of occipital tumour, and in one case of a cyst in Broca's area. In all these cases there was an excess of protein in the cerebrospinal fluid beyond the amount usually found in thrombotic lesions. With or without loss of consciousness the somatic expression of an occipital fit, in some of my cases, was characterized by repeated attacks of blindness lasting from seconds to minutes. But the psychological reaction preceded and succeeded the somatic process.

A woman, age 64, fell on the pavement, as a result of which her left forehead was bruised and her left eye discoloured. She was unable to relate what had happened to her when she returned home a hundred yards away. The following morning she was in a comatose state and when she recovered she complained that she had lost her sight for a short time. The same week she was seen by a local ophthalmologist who diagnosed detachment of the left retina and lens. A fortnight after the accident she appeared to

have recovered, but she complained of periodic attacks of loss of sight and her relations noticed that she was at times so drowsy that she could not be roused. One evening, two months after the accident, she 'collapsed' in her home. This was followed in the morning by headache and vomiting which continued on and off for three days. On her admission to hospital there were left homonymous hemianopia and loss of postural sense on the left side. No other organic signs were discovered. The retina and lens appeared to be normal. The cerebrospinal fluid showed 0·1 per cent. protein, and slight excess of globulin, but no other abnormal changes. She frequently complained of 'blackness before my eyes when I feel awful.' Headache was not once complained of and she denied its existence. A fortnight after her admission she was

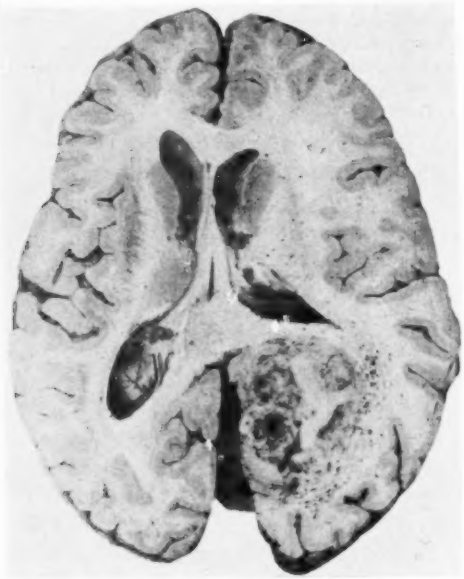

FIG. 3.

trephined over the right occipital region, by Mr. Wakeley. Figure 3 shows a leptomeningioma, found in this case at autopsy.

A bricklayer, age 55 years, was discovered unconscious on a scaffold 20 feet above the ground. An accident was inferred, but details were entirely lacking. He was taken to an infirmary nearby, where he recovered in three days and was sent home. A fortnight later he went into the country to recuperate and remained there for three weeks. When getting off the train at Paddington on his return home he 'collapsed' and thereafter was regarded as having lost his memory. Three months later he was sent to hospital as a case of 'loss of memory following an accident.' An examination revealed sensory aphasia. It was difficult to obtain his interest, because with one hand covering his forehead he kept repeating 'Oh dear.' There were no pyramidal signs. The sensory system could not be tested. When the light of an ophthalmoscope torch was placed at a good range to his left, his gaze invariably moved at once towards the light; but this never occurred when the light was placed

to his right. It was only when the light moved from the right inwards as far as to reach the nasal field that his gaze was directed to it. He was admitted as an in-patient. The cerebrospinal fluid contained 0·2 per cent. protein, and globulin in excess; all other tests were negative. A fortnight after his admission Mr. Tanner performed a left occipital decompression, and exposed a large tumour which extended forwards into the sensory area. A section of the growth showed carcinoma.

Of the remaining cases, the following presented the most interesting feature. A right-homonymous-hemianopic and partially sensory-hemiplegic patient, with a history of several hunting accidents and what had been diagnosed as two attacks of cerebral thrombosis, presented twice during a period of observation the following fit: his eyes rolled up and slightly to the right in tonus, then with head slightly flexed forwards the lids went into momentary clonus. The clinical picture somewhat resembled the reaction of the upper lids to the removal of a bit of grit or smoke blowing into the eyes, but there was in addition a total lack of conscious expression in his face for over one minute. The convulsive part of the attack, on both occasions, lasted about five seconds. The patient had no recollection of its occurrence, but, although uncommunicative on the subject, he was able to recall that 'everything went black.' When the nurse was asked if she noticed what had happened she replied: 'Oh yes, he is always getting neuralgia in his eyes like that.' Thereafter it was possible with the help of members of his family, who regarded this sign as a 'disagreeable habit,' to trace the existence of these attacks for a period of five years at least. Mr. Tanner and Mr. Dickson Wright exposed but did not remove a large left occipital tumour.

A male, age 38 years, was admitted to hospital with complete right hemiplegia and motor aphasia. 'Yes' and 'No' were the only words he could utter, not always relevantly. There was no papilloedema. Pyramidal signs were present on the right side and there was marked loss of sense of position when he attempted to touch any part of his paralysed side with his left index finger. Previous to his admission he had remained in bed in a London hospital for two months, where, according to the notes supplied, his case was diagnosed as one of cerebral thrombosis. The cerebrospinal fluid was found to contain 0·06 per cent. protein, excess of globulin, and 12 lymphocytes. After his admission his wife supplied the information that seven years previously he met with an accident on his bicycle, as a result of which he remained in a local hospital for three weeks with concussion. Shortly after the accident he would at times lose the power of speech for a few seconds, and she added that his present state began with an epileptic fit which 'left him paralysed on the right side, and speechless.' In view of the excess of cells in the cerebrospinal fluid an abscess was suspected and Mr. Colledge decompressed over Broca's area. A cyst, from which 2 oz. of fluid were removed, was there found attached to the pia. There was no abscess.

CRANIOCEREBRAL REACTION TO VIOLENCE

A short reference to the history of the reaction of the skull to violence is perhaps worthy of note. Hippocrates observes: 'For what is pressed inwards is broken off from another bone which continues in its natural state, and the "esphlasis" must necessarily be accompanied by a fissure.' Celsus says: 'Sometimes, though rarely, it happens that the bone remains sound and entire, whilst in consequence of a blow some vein ruptured in the membranes of the brain discharges some blood internally, which, stagnating there, excites some violent pains and in some produces blindness.' This, by the way, is the first recorded reference to subdural hæmatoma. He further states: 'If the fissure is not manifest, ink is to be laid upon the bone and

afterwards abraided by a rugine, in which case the fissure, if there be any, will retain part of the black substance.' James, in presenting the views of his time, remarks: 'It appears from geometry that among figures of equal perimeters the circle comprehends the greatest space. But the figure of the cranium is nearly spherical and therefore if it be pressed inwards its capacity must be diminished. Whether, therefore, the convex figure of the cranium be changed by intropression without fracture, or the fractured bone be forced from its place, the effect will be the same, which is compression of the brain.' The observations of Wilfred Trotter mark a new era in the advance of knowledge of head injuries. Trotter regards the skull as an elastic structure capable of being distorted in part or as a whole as the result of a blow on the head. He emphasizes the fact that the absence of fracture is not evidence that the skull has not been considerably distorted and the brain seriously damaged.

PERSONAL EXPERIMENTS

The elasticity of fresh skulls representing eight decades was tested as follows. The sawn rim of the vault of the skull to be treated was fixed on a block of lead 8 in. in diameter and 4 in. thick. A glass tube 36 in. long and $\frac{3}{4}$ in. in diameter was, by means of an iron stand fitted with adjustable brackets and clamps, firmly held vertically over the vault and just free from touching it. A magnet connected to a galvanic battery was fixed inside and at the upper end of the tube (fig. 4). Balls of hard steel, of various weights ranging from 14 gr. to 1 gr., were at different times fixed to the magnet and released from it by means of a switch on the battery. The balls after impact on the skull rebounded inside the tube and the first or maximum of the particular series of rebounds was measured by means of an adjustable steel furl on the tube. Balls of all the weights used rebounded. The average maximum rebound of a 7 gr. ball was 12 in. However, in view of the curvature of the skull producing deflections of the ball against the inside of the tube, and of other difficulties in providing constants, the test was satisfactory only in so far as the balls always rebounded. The rebound was less from the skulls of the first decade than from adult skulls. When the balls were allowed to fall on the plastic lead base they remained where they fell without rebound.

Elasticity is that property by virtue of which an object recovers its original shape and dimensions when the straining force is withdrawn. The recovery from the strain on the skull, produced by the impact of the ball, is implied in the rebound of the ball and is explained as follows. When the ball comes into contact with the skull, a mutual action, consisting of a pair of equal and opposite forces, takes place between the two bodies. Of these one acts on the ball, the motion of which is changed by the skull; the other acts on the skull which moves against its inherent resistance or stress. At the instant the two come into contact (*a*) a sound is heard due to oscillations;

and (*b*) the skull is strained, and begins to sink, and continues to sink through a space through which resistance of the skull is overcome by the ball. Thus, certain changes of figure and dimensions are produced in the skull. Because

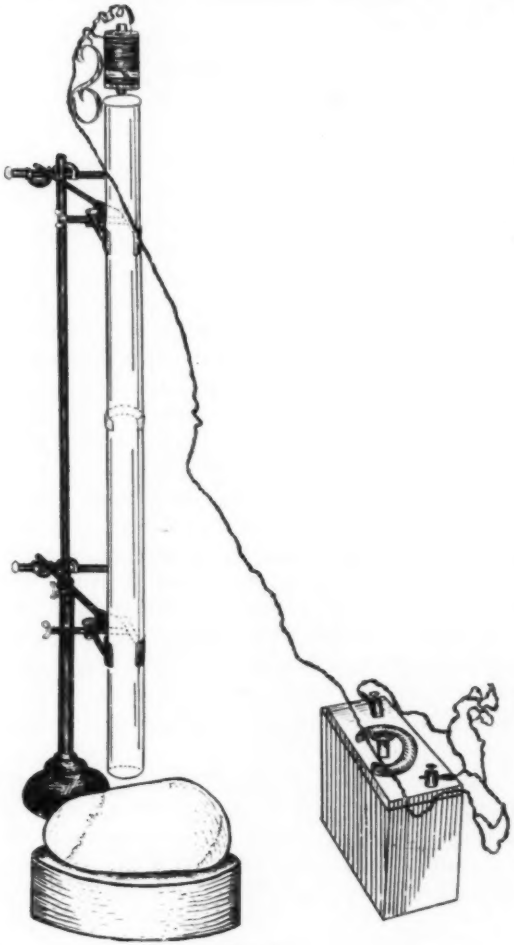

FIG. 4.

of its great hardness, deformity of the ball itself is negligible. The resistance of the skull to deformation increases from the instant the ball falls on it; it begins by being zero and increases until the velocity of the ball is wholly destroyed. For an instant the ball and the skull are at rest. Then the skull returns to its original form and by so doing tosses the ball from its surface.

The total height through which the ball falls is therefore 36 in. plus the amount of sinking of the skull at the point of impact, that is the space through which resistance is overcome. The amount to which the skull is capable of sinking within the limits of its elasticity is not known. It is probably very considerable.

CONCLUSIONS

In head injuries the skull is by no means fixed. Among other joints the craniovertebral joint permits the head to be pushed out of the way as a first defence against the full force of the wounding load on the skull itself. Yet even the smallest load (a ball of hard steel of the lightest weight) which acts on the skull produces an alteration of dimension or form.

An object falling on the head falls in a straight line ; then, if the injury is non-penetrating, the skull itself becomes the wounding body of the brain. However, instead of being a moving body going to the brain in a straight line, the circumference of the skull is constrained to injure the brain in the circumference of a circle. In the cases referred to, the tumours were situated in the cortex in parts remote from the head injury.

Into what shape then is the skull thrown when it is deformed by a head injury ? An answer to this question resolves itself into a geometrical conception of the shape assumed by a spherical body which is elastic and which when strained by a blow begins to sink, and continues to sink through a space through which its resistance is overcome. Sinking of the skull will tend to diminish the intracranial capacity and so to crush the brain as a whole.

It is, therefore, suggested that when a cerebral tumour also occupies the brain-containing space, a head injury will tend to crush the intracranial contents beyond the amount due to the sinking of the skull alone acting on a normally contained cavity. Thus, in cases of cortical tumour, it would appear reasonable to regard a head injury, *however slightly it acts on the skull*, as being a possible mechanical factor capable of precipitating the onset of epilepsy.

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Short Notes and Clinical Cases

THE BODY TYPE OF THE GENERAL PARALYTIC

By

ARTHUR GUIRDHAM

That the study of personality types initiated by Aristotle and Hippocrates was almost totally inhibited by the development of the germ theory of disease is nowhere shown more graphically than in the study of the reaction of the individual to the parasite of syphilis. Here is a disease the ubiquitous manifestations of which lend themselves to a consideration of the different types of subject afflicted at the different sites of selection. A particularly fruitful source of study should be that small percentage of the infected in whom the central nervous system is diseased. The theory of a neurotropic virus, a favourite preoccupation of the French school, has obtained little credence here. The increase in our knowledge of inherent immunities justifies our expressing the view that the infection of the central nervous system is at least as likely to be due to an innate susceptibility on the part of the individual as to a variability in the causative organism. Yet, while the responsible parasite, and the cytological changes it causes, have been studied so that the phenomena associated with them can be considered well established, little consideration has been given to that personality which must surely play a part, seeing how small a percentage of syphilities develop the diseases in question.

As to the determining influence which directs the attack of the spirochæte on the central nervous system, little is known. Perhaps more interesting is the speculation as to what innate constitutional peculiarity decides whether the victim becomes a paralytic or a tabetic. The mere statement that the point of attack of the virus is different in the two cases would be sufficient if dementia paralytica were merely a collection of haphazard neurological signs. But it is becoming increasingly held nowadays that the incidence of general paralysis of the insane depends as much on the victim as the virus. A prepsychotic paralytic personality is described. One is able to discover a general high level of competence and 'drive,' even through the obfuscation of psychosis which the patients present on admission to a mental hospital. War experience showed a sudden elevation of the incidence of general paralysis in those exposed to the rigours of campaigning. A statement such as this requires most careful consideration. It should not be taken as evidence of the old theory that stress is to be regarded as an equal

coincident cause. General paralysis of the insane is almost peculiar in being a disease for which a well authenticated organic causation, i.e. the spirochæte, is demonstrable, yet where only a few of those infected develop the signs of the disease. In such a case as this, where the operation of sudden, wholly unusual stress, such as warfare, increases the case incidence, it is reasonable to suppose that its effect is in increasing some innate individual susceptibility, rather than to postulate such a vague and widespread factor as stress as a truly concomitant cause. Were this latter the case the incidence of general paralysis of the insane would be much greater than it is. These, and other factors, point to an inherent peculiarity of personality as being of significance in the production of general paralysis, and justify the study of the general paralytic from the totalist standpoint of the Marburg school. In this short notice one is dealing only with the possibility of there being a constancy of one of the body types, as of Kretschmer, in general paralytics.

I remember a former teacher of mine observing that, given the fact that a group of patients were suffering from these two diseases, it was possible to recognize the tabetics because of their more elongated and asthenic structure, and the paralytics in virtue of their more compact and pyknic structure.

In early days in a mental hospital the writer, visiting sick wards containing patients unfamiliar to him, amused himself by counting, by the exercise of vision alone, the number of general paralytics. The degree of accuracy attained was surprising. One realizes, however, that the enumeration of these patients depended largely on the recognition of that peculiarly emotionless yet ready pleasantry of facial expression which is seen in so many paralytics. But apart from this one had the further intuitive conception that general paralytics displayed, on the whole, a far greater breadth to height proportion, i.e. relatively greater pyknic value, than did tabetics.

PERSONAL INVESTIGATIONS

The inquiry of which this brief notice is given is concerned only with the physical scheme of the paralytics. Unfortunately no control group of tabetics is immediately at hand. In the group of paralytics quoted below, consideration was given only to those in whom the weight had been stabilized for several months.

The cases were investigated by means of height, weight, chest circumference index of Pignet, who quotes—in the three categories of pyknic, athletic, and asthenic—average values and ranges of variation for the index :

Height in centimetres—(weight in kilograms + chest circumference in centimetres).

The following result was obtained :—

TABLE I

	Pyknic	Athletic	Asthenic	Total
Number of subjects	10	10	7	27

As a check on these figures, measurements derived from Kretschmer's tables of typical measurements for the three main types are also utilized. It must be stated quite clearly that Kretschmer utilized no such index as Pignet's. It is just that, as a control, the Pignet index is being calculated from Kretschmer's average figures for height, weight, and chest measurement. This procedure is of value, because body-measurement figures in different communities are available. Average values derived from Kretschmer's measurements are given below, together with the usually quoted Pignet figures.

TABLE II

	Average values for Asthenic	Athletic	Pyknic
Kretschmer (derived from) ...	33·8	15·4	5·3
Pignet	34·3	11·9	—5·5

It is seen that the values for the athletic and pyknic categories give lower averages when derived from Kretschmer's figures. The proportion of the three types, employing these latter, is as given below :—

TABLE III

	Pyknic	Athletic	Asthenic
Number of subjects	8	14	5

The above figures were derived from both sexes, the males showing a preponderance of 17 : 10. The Pignet index is said to be less reliable in females, but the figures quoted below in Table IV (for females alone) show the same tendency, as in the whole group, to a deficiency of asthenic elements, while there is also a proportionately greater development of pyknic elements.

TABLE IV

	Pyknic	Athletic	Asthenic
Number of subjects	6	1	3

The figures derived from Kretschmer's averages are exactly the same.

So far then as what we might call an immediate view of the condition is concerned, dementia paralytica provides no clean-cut accentuation of a single body type. All that can be said is that there is a general paucity of asthenic types.

The most profitable line of study would be to estimate the body types according to the degree of deterioration present. Unfortunately, most of the subjects available were, in this respect, in a stationary condition. In two cases showing an unmistakable general deterioration extreme asthenic scores of 38·44 and 41·37 were recorded.

In 16 of the cases used in this investigation, the measurement indices obtained on admission were available. Of these only five displayed the same body type as on admission, and of these five only two showed any constancy

in their index figures, the others varying by 6, 9 and 9 units respectively. The interval of time between the taking of the two measurements averaged about three-and-a-half years.

In addition, on admission, there was a majority of cases of asthenic habitus, exactly the reverse of the position when the later measurements were taken. The proportions were :—

TABLE V

Pyknic	Athletic	Asthenic	Total
3	4	9	16

The considerable fluctuations of weight in dementia paralytica are seen to cause variations in the index to such an extent that no clear body type emerges. In these 16 cases the average between the index values on admission and at the present time was calculated. Such a procedure cannot claim any considerable accuracy, but at least it is of useful general indicative value. The results derived from it are as follows :—

TABLE VI

Pyknic	Athletic	Asthenic	Total
3	5	8	16

The divergencies encountered in every method of approach lead us to the conclusion that no clear body type emerges in general paralysis of the insane. Personality studies of this disease are not invalidated by such a finding. They must, however, be established from criteria other than those of Kretschmer. Nor do the findings given above necessarily contradict the observations of my teacher already alluded to. Certainly, according to the standards of mensuration, there is no major development of pyknic types ; but this does not preclude the possibility of general paralytics being relatively more pyknic than tabetics.

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TONIC PUPILS WITH ABSENT TENDON REFLEXES IN MOTHER AND DAUGHTER

By

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Numerous cases have now been recorded of the above condition, but the following are described as being unusual in that (*a*) the abnormalities occur in two relatives—mother and daughter; (*b*) the abnormality of the pupils commenced at approximately the same age in both cases, and as regards the pupil there has been no change in one case for 32 years.

Case I. Married woman, age 61 years. The left pupil was first noticed to be small and fixed following an attack of acute and severe tonsillitis at the age of 29 years. Neither the grandparents, the parents, the husband nor seven siblings have shown inequality of the pupils.

At the age of 36 years, the patient was examined by Dr. R. J. Coulter, of Newport, Monmouthshire, who kindly informs me that he found that the left pupil was quite inactive to accommodation or direct light, but showed a very doubtful consensual reaction.

Upon examination 25 years later, at the age of 61 years, the left pupil showed no reaction to light, either directly or consensually. The reaction to accommodation was doubtful. Slight irregularity was present. The right pupil reacted normally, including consensually. Discs were clear with marked physiological cups, although the edges were somewhat illdefined all round. Visual fields were normal. Ocular movements were good and movements of face, tongue and palate were normal.

Biceps, triceps and supinator reflexes were present and equal upon the two sides but the left kneejerk and both anklejerks were absent. The right kneejerk was obtained on reinforcement only. There were no subjective symptoms in the eye or the legs.

Case II. Married woman, daughter of above, age 37 years. At the age of 33 years, following an attack of acute pyelitis, the pupils were found to be unequal.

Upon examination four years later, at the age of 37 years, the left pupil was smaller than the right and slightly irregular. There was no reaction to accommodation and none to direct light. A slight consensual reaction of a slow type was present. The right pupil reacted well, including consensually. Discs were clear with well-marked physiological cups, but with slight indistinctness of edges. Ocular, facial, tongue and palate movements were normal. Biceps, triceps, and supinator reflexes were not obtained. The left kneejerk was absent. The right kneejerk was also absent, but paresis from acute anterior poliomyelitis had occurred in this leg at the age of 12 years.

SUMMARY

1. Two cases of tonic pupils are described occurring in the left pupils of mother and daughter.

2. The inequality of the pupils was first noticed in the mother at the age of 29 years and in the daughter at the age of 33 years.

3. The inequality of the pupil in the mother has been present for 32 years.

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Editorial

NEUROLOGICAL THERAPEUTICS

IT has occasionally been said of organic diseases of the nervous system that while constituting a most interesting field of study in applied physiology and pathology, they are therapeutically destitute. An ardent neurologist might have replied that treatment in organic neurology at all times compared favourably with that in organic medical diseases, such as chronic conditions of the heart, liver and kidneys. We utter a truism in adding that all advance in knowledge of the ætiology, pathology and diagnosis of a disease inevitably leads to increased understanding of the possible means of treatment. It is to these aspects of organic disease of the nervous system that most neurological research has been directed, with many brilliant results. Nevertheless, in reviewing the progress of neurology during recent years, it is evident that increasing attention has been paid to treatment per se and that the advances have been considerable. Several diseases, formerly considered almost untreatable apart from general care and management, are now subjected to direct attack.

Foremost among these is that form of progressive syphilitic meningoencephalitis, popularly though unfortunately known as 'general paralysis of the insane.' The application of malarial therapy undoubtedly inhibits the malady in the majority of early cases with the result that after a number of years, varying from two to six, the cerebrospinal fluid becomes normal, losing its increased protein content, positive Wassermann reaction and Lange curve. Patients are known among the first to be treated in this country—some 14 years ago—who still survive and in some instances remain useful members of society. An average of the available statistics indicates that approximately 35 per cent. of all cases treated—irrespective of the stage of the disease—show good and lasting remissions, while in a fair proportion of the remainder improvement or arrest of the disease occurs. Compare this with the prognosis invariably given prior to the introduction of malarial treatment

—that following a progressively increasing dementia the disease would prove fatal within three years.

The prognosis with malarial therapy varies with the stage of the disease at which it is possible to apply the treatment—the earlier in the malady, the better is the outlook. Many cases, however, do not come under observation until they are admitted under certificate to a mental hospital and when the brain may have already suffered irreparable damage. For this reason statistics confined to early cases would show an even higher recovery rate. Many factors in the treatment still await further elucidation. For instance, what is the exact mechanism by which malaria counteracts the syphilitic disease? Is improvement in the latter due to leucocytosis, pyrexia, antibody-formation, increased metabolic action or general vasodilatation? As far as our present knowledge goes, increase in the large mononuclear cells and possibly the occurrence of an immunizing reaction against the stroma of destroyed red blood corpuscles appear to play a considerable part. Again, from the clinical aspect, why do some cases—even early in the disease—fail to react to malaria therapy and why do others eventually show negative Wassermann reactions in the blood and cerebrospinal fluid and yet deteriorate clinically?

Other methods of inducing pyrexia have also been tried, such as relapsing fever, various bacterial vaccines injected intravenously, saprovitan, injections of milk, sulfosan and radiothermy (electropyrexia), but malaria therapy still appears much superior to all. As regards radiothermy, claims have already been made that the method is at least equal to malaria in its immediate clinical results. Further observations a few years hence, however, will decide this question. At the outset, the claim must be received with reserve, as the benefit in degenerative syphilitic encephalitis accruing from malaria therapy appears not necessarily to depend exclusively on the pyrexia, good results having been reported by Wagner-Jauregg and others when the induced malaria has been entirely or almost afebrile.

Another organic disease viewed until recently with comparative therapeutic helplessness to which it is now possible to apply some direct treatment is progressive muscular dystrophy. Many years ago the observation was made that the urine of patients suffering from myopathy contained creatin—a substance not excreted under normal conditions. It would appear that the muscles affected by the dystrophy are unable to retain creatin, whether of exogenous or endogenous origin.

The administration of an amino-acid in the form of glycine or glycocoll was found to give rise to definite clinical improvement. Its mode of action is probably twofold : by promoting creatin formation, and by enabling the muscles to retain and metabolize the creatin. The chief obstacle to a widespread application of the treatment is the present high cost of the substance glycine, large doses varying from 10 to 30 gm. a day being necessary. Glutamic acid or monosodium glutamate may be used as substitutes, and gelatin contains 20 per cent. of glycocoll. Treatment with the latter in doses of 100 gm. per day given with orange or lemon juice is worthy of extended trial at relatively small cost.

Again, the institution of treatment as early as possible in the course of the disease is essential, as improvement depends upon the condition of the muscle-fibres at the time treatment is started. Amelioration cannot occur in atrophied muscles in which the nuclei of the fibres are already disintegrated and no form of treatment could be expected to prevent further degeneration. There can be no question concerning the initial improvement in cases of myopathy treated with glycine, but it remains to be seen how far this therapeutic method is able to avert the usual progress of the malady.

The recent discovery that injections of physostigmine and its analogue prostigmin lead to temporary abolition of the muscular weakness in myasthenia gravis is distinctly encouraging. It has also been found that atropine given at the same time as the prostigmin prevents the colic and nausea resulting from the latter substance without impairing its action on the muscles. The optimum dose of prostigmin appears to be 5 c.cm. (2·5 mg.) given with 1/100 gr. of atropine. Improvement in the affected muscles begins in about one hour and lasts up to six hours, and two injections a day may be given. The effect of the prostigmin is said to be due to its property of delaying the destruction of acetylcholine at the motor nerve-ending by the choline esterase normally present in the blood. If it is a fact that nervous impulses set free acetylcholine or some analogous substance at the nerve-endings, it would appear that in myasthenia gravis there is an insufficient supply of this substance. Prostigmin, by delaying the destruction of acetylcholine, tends to compensate for the deficiency.

On this hypothesis, defective innervation resulting from a disability of the lower motor neurone—whether in the anterior horn cells, in the nerve-fibres or in the nerve-endings—should tend to be compensated by an injection of prostigmin. From

experiments in cases of neuritis and anterior poliomyelitis this indeed appears to be the case. Consequently, an even wider field of experimental therapeutics is revealed.

It might be said that it is inconvenient to give a patient one or two hypodermic injections each day. Nevertheless, it is routine in diabetes for the patient to measure and inject his own doses of insulin; sufferers from myasthenia may similarly be educated to give their own injections of prostigmin and atropine.

As with glycine, the cost of prostigmin is a difficulty, and various substitutes have been suggested and tried—e.g. physostigmine salicylate in doses of from $\frac{1}{8}$ to $\frac{1}{6}$ gr. given in water by the mouth and preceded by 15 to 20 minims of tincture of belladonna. In the hands of one observer this method was said to be followed by improvement in 20 minutes, reaching a maximum in from one to two hours and lasting about five hours. Some faintness and a weak pulse during the first two hours were concomitant symptoms. It is evident that individual patients have different degrees of tolerance to physostigmine by the mouth, as other observers failed to observe the improvement in myasthenia from this method while noting epigastric pain, chilliness, nausea, vomiting and a weak pulse in the cases treated. Potassium chloride in large doses (10 to 12 gm.) given by the mouth in a tumblerful of water has also been tried. The use of this substance is based on the observation that it has a stimulating effect on ganglion cells and that it raises their excitability to preganglionic stimuli and to acetylcholine. Improvement in the myasthenic symptoms lasts about two hours. Diuresis occurs constantly after each dose of the potassium chloride and unpleasant symptoms may be nausea and mild diarrhœa. In smaller doses, however, it may serve as a useful adjunct to prostigmin treatment, as some patients complain of undue fatigue after the effects of the latter substance have worn off. A dose of from 4 to 6 gm. of potassium chloride taken shortly before the action of prostigmin has passed relieves the feeling of exhaustion and tends to prolong the period of improvement.

Idiopathic narcolepsy is yet another disease of the nervous system to which improved treatment is now applicable. The use of ephedrine in this disorder was a distinct advance on the older methods of prescribing caffeine and thyroid extract. More recently Prinzmetal and Bloomberg in America have reported even better results with benzedrine sulphate. This

substance is related both to epinephrine and ephedrine and has a greater stimulating effect on the central nervous system than the latter. It is further of comparatively low toxicity. Almost complete relief of the narcoleptic attacks occurred in every instance of the disease treated, with considerable improvement in the cataplexy when present. Using control cases, the authors named considered that benzedrine was three times as effective as ephedrine and that even small doses of the former produced complete relief of symptoms in cases which were not relieved by large doses of ephedrine. The dosage of benzedrine varies from 10 to 30 mg. morning and afternoon, with a smaller dose early in the evening according to the effect on the normal night sleep. Further experience confirms the claims made for this substance in narcolepsy; indeed, it is usually advisable to omit the evening dose owing to the development of nocturnal insomnia.

From the observations made above, it may be deduced that the immediate future of therapeutics in organic neurology lies mainly in the researches of biochemistry and experimental pharmacology.

Abstracts

Neurology

NEUROANATOMY AND NEUROPHYSIOLOGY

[145] **The localization of the macular fibres in the optic radiations** (Zur Lokalisation der Maculafaserung innerhalb der Sehstrahlung).—A. JUBA. *Zeits. f. d. g. Neurol. u. Psychiat.*, 1935, **154**, 123.

RETROGRADE degeneration, almost exclusively involving the macular region in the geniculate body, resulted from unilateral softening in the area striata affecting mainly the polar region. The fibres situated in the ventral part of the vertical peduncle in the optic radiation were degenerated. Thus, these fibres have to be considered as the fibres of central vision in the optic radiation. The case described favours a theory that the macular fibres are situated in the middle of the optic radiation and not in its dorsal part as Pfeifer had maintained.

M.

NEUROPATHOLOGY

[146] **Clinical examination of the intestinal tract in cases of encephalitis lethargica relieved by atropine** (Klinische Untersuchungen über das Verhalten des Magen-Darmkanals bei mit Atropin behandelten Encephalitikern).—H. FEHSENMEYER. *Münch. med. Woch.*, 1935, **82**, 1723.

SIEGMUND described important anatomical alterations observed at autopsy in cases of encephalitis lethargica which had been treated by atropine over long periods. The author of this paper reports clinical cases of this disease treated in the same way. She observed similar disturbances, and considers that a disturbance of the function of the autonomic nervous system results from Parkinsonism, the consequence being disordered gastric function. Sympatheticotonus became predominant by use of atropine and a permanently diminished mobility of the whole intestinal tract resulted. This means that atropine treatment per se is not to be regarded as the primary cause of the alterations in the intestinal tract observed by Siegmund as well as by Fehsenmeyer.

M.

SENSORIMOTOR NEUROLOGY

[147] **Blindness for form resulting from a lesion of the occipital lobe of the brain** (Über Form und Ortsblindheit bei Verletzung des Hinterhauptlappens).—K. KLEIST. *Deut. Zeits. f. Nervenheilk.*, 1935, **138**, 206.

INJURY to both occipital lobes of the brain was a result of a gunshot lesion affecting the posterior part of the skull. As in other cases seen during the war a distinct localization was observed for different qualities of optic disturbance. Blindness for the form of objects was an isolated defect more definitely observed than in any case previously examined. Deficient perception of form and shape was limited to the visual sphere and no disturbance was observed with regard to form and shape in any other region of the brain, e.g. by touching, writing and drawing. Goldstein and Gelb previously described a disturbance for visual form not limited to the visual region in a case of a lesion of the occipital lobe, but according to Kleist's opinion this resulted from a brain lesion outside the visual sphere.

M.

[148] **Anatomical considerations in clinical interpretation of brain injuries.**—IRVING J. SANDS. *Amer. Jour. Psychiat.*, 1936, **92**, 771.

THE orbital plates of the frontal bones, the lesser wings of the sphenoid, and the restricted motion of the brain within its encasement are indirect contributing causes to brain injuries. Cerebral and subarachnoid hæmorrhage, cerebral œdema, and disorganization of the Virchow-Robin lymph system contribute to brain destruction and degeneration. Post-traumatic sequelæ are due to loss of brain tissue, meningocortical adhesions, contraction of scars, collection of fluid in the meninges, and interference with proper cerebrospinal fluid and lymphatic circulation. Significant brain injuries may occur without loss of consciousness. Conduct disorders following such injuries are to be differentiated from psychogenic behaviour disorders.

C. S. R.

Psychopathology

PROGNOSIS AND TREATMENT

[149] **The therapeutic use of dinitrophenol and 3 : 5 dinitro-ortho-cresol in schizophrenia.**—J. M. LOONEY and R. G. HOSKINS. *Amer. Jour. Psychiat.*, 1935, **91**, 1009.

THIS is a preliminary report on experiments made with 10 schizophrenic patients. Both drugs caused increase in the rate of oxygen consumption

with various other metabolic effects indicative of increased oxidative efficiency. The ortho-cresol proved to be the more potent but showed the property of causing discolouration of the skin and scleræ. The therapeutic results were indeterminate. Aside from discolouration of the integument by the ortho-cresol neither drug, within the limits of dosage used, caused any perceptible harmful effects.

C. S. R.

[150] **An investigation into the after-history of 90 patients discharged from a mental hospital against advice.**—Louis Minski. *Jour. of Ment. Sci.*, 1935, **81**, 509.

Of 90 patients who left the Maudsley Hospital against advice, 17 could not be traced, 25 were in mental hospitals, 24 recovered, 16 were at home no better, seven committed suicide, and one died at home. Obviously the standards of behaviour determine the relatives in taking patients home, and for this reason the largest number taken home whilst still ill were suffering from depressive states, where behaviour likely to lead to conflict with the environment was not marked. In view of the high proportion of suicides it would seem necessary to urge relatives of patients suffering from severe depressive states to send them to suitable hospitals. Most of the depressives who remained at home, although ill, were of the involutional type, and only two who might reasonably be expected to recover remained ill in difficult home situations. The relatives seemed to take a more serious view of states with excitement; only four manics and three toxic confusional patients were taken home whilst excited; no unrecovered schizophrenic patients remained at home.

C. S. R.

Reviews and Notices of Books

The Origins of Love and Hate. By Ian F. Suttie, M.D. With a preface by Dr. J. A. Hadfield. London: Kegan Paul. 1935. Pp. 275. Price 10s. 6d. net.

DR. IAN SUTTIE has been a contributor to this JOURNAL in days gone by, and his numerous articles on psychopathology have shown him to be possessed of a well-stored and critical mind. These features are seen in the reasoned and animated criticism with which he here assails Freudian theory. He adduces evidence to show that Freudian theory has from the outset been coloured by the temperament of Freud himself; from Freud's own lips Dr. Suttie illustrates a 'specially inexorable repression' that has resulted in a grudge against mothers and a mind-blindness for love. Mother attachments of the individual are, for Freud, 'lost in a past dim and shadowy,' and the Mother-Cults of antiquity are for him a repellant and insoluble mystery. In temperate language and with incisive argument Dr. Suttie proceeds to exemplify this bias on the part of the founder of the theory—a bias of which others have been aware and which, unfortunately, has reproduced itself in not a few of his disciples. It has found perhaps its crudest expression in such a statement as 'Every mother is her child's first seductress'—an opinion so monstrous as to prove of itself that its originator is incapable of understanding what maternal love means. It is good indeed that someone has been found who is so well equipped as Dr. Suttie to cross swords with the exponents of ill-considered views of the kind.

But there is much more than destructive criticism of Freudian theory in this finely written work, in which the meaning, psychology, function and expression of love are constructively discussed with scientific insight and a large measure of sound common sense. Love is, properly, separated and distinguished from appetite and desire, and cultural interest is shown to be something very different from substitute sex gratification.

Objective and Experimental Psychiatry. By D. Ewen Cameron, M.B., etc., Physician-in-Charge, Provincial Mental Hospital, Brandon, Man. New York: The Macmillan Company. 1935. Pp. 271. Price 12s. 6d.

THE general tenor of Dr. Ewen Cameron's argument is that psychiatry has been loaded with rubble from the past more than any other department of science, that the era of mere observation is passing, that only experimental and quantitative psychiatry is calculated to interpret human behaviour aright and ensure ultimate victory over mental disease. Lack of an 'experimental animal' has been and continues to be a great drawback of the experimental

method as applied to human psychiatry, so that observational methods must continue awhile, but, using them, we must combat with rigour any development of 'projectionism.' The author then proceeds to describe and discuss intelligence tests, introversion and extraversion, word association tests, heredity, conditioned reflexes, and sundry other topics concerned with the objective investigation of the body tissues in mental disease. The chapter on pathology is less satisfactory, for while he says well that 'the focus of the main attack will continue to be the thing that lives and moves rather than the footprints which it leaves behind' he also seems to hold that biochemistry and physiology have benefited 'at the expense of pathology.' The truth surely is, that no method of approach should be ignored and that pathology has its contribution to make just as much as any of the others.

Emotions and Bodily Changes. By H. Flanders Dunbar, M.D. New York: Columbia University Press. London: Humphrey Milford. 1935. Pp. 595. Price 25s. net.

THIS closely printed volume embodies a survey of the literature on psychosomatic relationships of the years 1910 to 1933. We do not know whether to admire more the ability with which the bulky material is handled or the skill with which it has been gleaned. An appendix contains some 2,250 bibliographical references, and an index of authors' names covers over 20 double-columned pages. No digest of the huge collection of data is attempted, but at the same time each division or subdivision is briefly discussed as the matter runs on, and there are various introductory paragraphs dealing with earlier contributions to a particular topic than those of the period mentioned above. It is not unfair to say that, on the whole, the standpoint of the author himself leans to a psychogenic interpretation of various phenomena with which, for example, the 'organic neurologist' may be concerned; he speaks of studies which 'represent a regression [sic] to the point of view of localization' so long as they attempt to replace 'our actual knowledge of dynamic psychopathology' by 'physiological or brain-anatomical assumptions.' Many will consider that the shoe is precisely on the other foot, and that psychopathological 'assumptions' are offered freely in place of 'actual anatomical and physiological knowledge' of the brain.

Destiny and Disease in Mental Disorders. By C. Macfie Campbell, M.D., Professor of Psychiatry, Harvard Medical School. London: Chapman and Hall. 1935. Pp. 207. Price 10s. 6d. net.

THE well-known Medical Director of the Boston Psychopathic Hospital has in this engagingly written volume dipped into his casebook and given us a series of documents of troubled lives, whose outstanding interest lies in the fact that, as he says, they reveal the working of the deeper forces within man which in health are concealed. They show human personality

'grappling with the special difficulties of its individual destiny.' That Professor Macfie Campbell should thus underline the existence of personality conflicts in the psychoses, of complex forces at work below the surface, does not ipso facto mean he belittles the attainments of other modes of research with the same material; he merely claims in so many words that the guinea-pig as a personality is limited. Many of his reports are dramatic in their setting and emphasize the need for passing beyond academic considerations when the mind diseased is the subject of study. All who read the book will feel indebted to Professor Macfie Campbell for his sympathetic insight into and judicial analysis of the complicated motives and movements that make up the tragicomedy called life.

The Problem of Mental Disorder. Edited by Madison Bentley. New York: McGraw Hill Publishing Co. Ltd. 1934. Pp. 388.

This book seeks to review the present position of knowledge in relation to psychiatry and to indicate the lines along which research ought to proceed in order to extend that knowledge.

After a review of the problem which is being investigated five prominent American psychiatrists indicate their point of view. Dr. Macfie Campbell deals with that of clinical psychiatry, Dr. Myerson with that of medical psychiatry, Dr. Wechsler with that of neurology, Dr. Adolph Meyer with his own psychobiological standpoint and Dr. Kubie with the standpoint of psychoanalysis. These authorities not only explain their own approach but try to show how future work along their own chosen lines will still further extend knowledge. The general impression from this section confirms what is a fairly general opinion, viz. that psychiatry is in a state of serious confusion and that the whole subject needs coordinating and pulling together; and moreover that the lacunæ in our knowledge are perhaps more obvious than the positive achievements.

In the final section contributions are made from what are called the supporting sciences. The first eight of these deal chiefly with the anatomy and physiology of the nervous system and again the disproportion between what we know and what we would like to know is all too obvious. The next six deal with topics of general physiology and medicine; finally there are chapters on psychology, sociology, anthropology and education.

Like all books of this kind which are written by many different authors from as many different points of view there is a lack of coherence and unity, but the editor has sought to remedy this by summaries and conclusions at the end of each section and much information is to be obtained from the various articles by the psychiatrist who studies them carefully. If at the end of his study he feels a sinking of the heart that there is so much that we still have to learn if we are to pretend to understand the working of the human mind in health and disease it will not be surprising; but after all what makes neurology and psychiatry such an entrancing study for the inquiring mind

is that so little is known and that the subject presents many chances for original observation and inference. At least it is clear that generations will have come and gone before all the lines of research which are adumbrated in this book have been followed to a successful conclusion.

This book will serve a useful purpose if those interested in psychiatry and medical psychology can learn from it that their own approach is not the only one and that scientists of all varieties are interested in the problem of the working of the mind and are slowly—perhaps very slowly, but we hope surely, converging towards the light. Let everyone acknowledge that all these approaches are useful and by no means mutually exclusive and perhaps the pace of advance will be accelerated.

Untersuchungen über die Fruchtbarkeit gewisser Gruppen von Geisteskranken (Schizophrenen, Manischdepressiven und Epileptikern). By Erik Essen-Möller. Acta Psychiatrica et Neurologica, Supplementum VIII, 1935. Pp. 314.

THIS statistical study is based on an enormous number of investigations carried out at the Kaiser Wilhelm Institut für Genealogie und Demographie in Munich; some 50,000 data concerning some 20,000 individuals were collected and analysed. Among the general conclusions the following may be specified.

Manic-depressives show reduced frequency of marriage and increased mortality-rate after their illness has begun, as compared with those of the rest of the population; but these factors affect the dissemination of the disease little, for the age at which symptoms begin is late rather than early. Schizophrenes are a diminishing quantity as contrasted with the rise in general population; this depends on their low marriage-rate and relatively early age for symptoms to begin; their highish mortality-rate matters less. Epileptics increase in relative number just as little as schizophrenes, in part at least because of the early appearance of symptoms and the low marriage-rate. Among other topics discussed at some length is the bearing of compulsory sterilization on the spread of psychoses; the statement is made that it will act very slowly indeed, yet reduction of manic-depressives and schizophrenes will take place even more slowly without it.

Les Hydrocéphalies aiguës et subaiguës d'origine otique. By Robert Bourgeois. Paris: Masson et Cie. 1935. Pp. 178. Price 33 fr.

THE most interesting part of Dr. Robert Bourgeois' monograph on what is sometimes termed 'otitic hydrocephalus' is the chapter devoted to pathogenesis. Rejecting, or at least adversely criticizing, the theories of collateral œdema and of anaphylaxis, he argues that in typical cases the lesions depend on pure vasomotor disorder. Traumatic cerebral œdema may exist without any fracture of skull or meningeal hæmorrhage and is often seen in com-

motional states, after operation for cerebral tumour, etc. As in his cases of hydrocephalus due to ear trouble, the process begins by oversecretion of cerebrospinal fluid, next by the addition of cerebral œdema and venous stasis, which depend on a vasomotor reaction. In the event a mechanical factor adds to the complexity of the pathological situation. Venous stasis alone, in his view, is insufficient. The original oversecretion of fluid is caused by vasodilatation of the choroid plexuses. On the clinical side three varieties are distinguished—a diffuse external cortical type; an internal or encysted ventricular type; and a posterior fossa type.

The monograph is complete in its survey of the field and has a good bibliography.

Genie, Irrsinn und Ruhm. By Dr. Wilhelm Lange-Eichbaum. Second edition, enlarged. Munich: Verlag Ernst Reinhardt. 1935. Pp. 542. Price RM.13.

In 1931 we reviewed in this Journal an English version of a smaller book by the same author entitled *The Problem of Genius*. The present work is the second edition of another study dealing more or less with the same topic but on a larger scale. In discursive fashion he roams over a field of interest to all educated readers, inter alia providing his list of geniuses—not of course intended to be exhaustive. The reviewer confesses his ignorance of many of the names, yet cannot refrain from expressing mild surprise at finding therein those of Marat, Oscar Wilde, Verlaine, Helen Keller, Amenhotep IV, Andersen (Hans Christian), Brougham, Poincaré—to mention one or two. Are celebrities or 'notorieties' also geniuses? Where is the line drawn between talent and genius? Numerous poets, musicians and artists crowd the catalogue, but scientific men of genius are scarcely alluded to, and not one in medicine, so far as we have noticed. Can the author be begging the question? For he alleges that the genius is neither a superman nor the forerunner of a race of more highly endowed and developed men; genius is not the rosy morn of a new day, but rather the setting sun, a melancholy going down. This contention it would be easy to controvert by choosing geniuses who were not, as many of those selected by the author, psychopaths and degenerates.

Child Psychiatry. By Leo Kanner, M.D., Associate Professor of Psychiatry, The Johns Hopkins University, Baltimore. With prefaces by Professor Adolf Meyer and Professor E. A. Park. London: Baillière, Tindall and Cox. 1935. Pp. 527. Price 27s.

It is a good thing to have a textbook of child psychiatry, and Dr. Kanner is to be congratulated on the conception and the execution of his task. Various other aspects of children's diseases and ailments have had their exponents, and as regards psychiatry Dr. Kanner is the first to admit that he has had

forerunners in the field. His compendious volume however is planned on an ambitious scale and has an up-to-date outlook which adds to its value. He advocates an approach from the standpoint of psychobiology, and dreads what he calls 'terminological strait-jackets.' Behaviour disorders are not easily formulated in terms of 'disease-entities.' True though this is, thought is none the less apt to become rather 'woolly' when the 'problem' presented by the child is considered to be the 'diagnosis.' 'Reaction-tendencies' or 'reaction-patterns' may be popular words, but whether they aid in the hunt for causation and localization is another matter. The author is led to subdivide his 'diagnoses' by describing 'anergastic,' 'dysergastic' and 'oligergastic' reaction-forms. He asserts that 'there is a sufficiently large group of idiotic and imbecile children in whom neither an abnormal brain condition, nor an abnormally shaped skull, nor an unusual endocrine or metabolic pathology can be found'; this claim we do not accept, nor the further allegation that defective intelligence can exist without anatomical substratum.

Die Seelenstörungen der Blutdruckkranken. By Privatdozent Dr. E. Krapf. Leipzig and Vienna: Franz Deuticke. 1936. Pp. 120. Price M.6.

THIS essay on the mental symptoms of hypertensive states is written principally for the psychiatrist, by whom it is likely to be appreciated. After a description of manifold symptoms of a psychopathological kind attributable in the author's opinion to hypertension and ranging from 'blanks' or 'absences' to alteration of personality, an attempt is made to explain their pathogenesis and several alternative theories are discussed. Another division of the book deals with psychoses of the involutional period and their relation to hyperpiesis.

The general impression left on perusal is perhaps that the author has not altogether established a causal nexus between symptom and blood-vascular state, in the sense that allowance is not always made for the possibility that the two coexist in elderly persons without being integrally associated. That twilight states, poriomania, anxiety, hallucinosis, the Ganser syndrome, amentia, delirium and so forth are found in patients having hypertension must naturally be accepted, but the latter may be only one factor of several, and that not the most important.

Les Astéréognosies. By J.-P. L. Delay. With a preface by Professor G. Guillain, and 19 illustrations. Paris: Masson et Cie. 1935. Pp. 548. Price 65 fr.

AN elaborate, original, and well-planned study of the subject of astereognosis takes the reader farther into problems of neurophysiology and psychology than the title indicates. Dr. Delay properly distinguishes two principal

varieties of astereognosis ; the first is due to defect of analysers (in Pavlov's terminology)—that is to say, the person concerned fails to recognize objects by touch because the function of his receptors is impaired ; in the second the latter is intact, the error or fault being one of tactile asymboly. For the analyser defect of intensity the term ' ahylognosis ' is coined, for defect of extensity the word ' amorphognosis.' When one or other kind of anæsthesia is instrumental in producing astereognosis the localizing value of the latter is virtually nil. When the phenomenon is conditioned by analyser defects themselves associated not with anæsthesia but with perceptive agnosia, i.e. where the defect is central, then the symptom has a cortical origin and possesses localizing value. In the third place, when no analyser malfunction will account for the symptom, it becomes a tactile asymboly and is exclusively cortical as regards the underlying mechanisms.

Many abridged case-reports from the literature and a number of personal cases enhance the value of the work, which demands and will repay careful reading.

The Clinical Aspects of Visceral Neurology. By W. K. Livingston, M.D., Clinical Associate in Surgery, University of Oregon Medical School. London : Baillière, Tindall and Cox. 1935. Pp. 254. Price 22s. 6d.

The purpose of Dr. Livingston's monograph is to describe those morbid conditions that have been shown to benefit by resort to visceral nerve surgery. Concise introductory chapters deal with the anatomy, physiology, and pharmacology of the autonomic system, and are succeeded by one on visceral pain and another on the regulation of bloodvessel function. The main thesis of the book is then reached, viz. the neurosurgical treatment of such conditions as Raynaud's disease, thromboangeitis obliterans, angina pectoris, pelvic disorders, and chronic arthritis. The rest of the volume is devoted mainly to surgical technique.

There are 46 figures in the text, which is clearly written and illustrated by a series of case-reports with discussions thereon.

La paraplégie flasque aiguë du cancereux : étude clinique. By Ernest Woringer. Strasbourg : Editions Argentoratum. 1935. Pp. 134.

In his thesis for the Doctorat en Médecine the author describes a rather special variety of acute flaccid paraplegia associated with malignant disease of the vertebral column ; at a time when all signs of carcinoma are latent, pains along the spine or transient heaviness of a limb are followed rather quickly by a flaccid motor and sensory paraplegia, transient increase of deep reflexes and perhaps a Babinski plantar response ; soon all reflexes are abolished and the plantar becomes flexor again. Of rapid evolution, and generally fatal, the syndrome cannot be due to compression, seeing that it

may develop although no growth has entered the spinal canal. The lesion is believed to be of toxic origin.

Synthèse des Voies de Conduction des Centres Nerveux. By E. Leblanc, Professor of Anatomy at the Faculty of Medicine of Algiers. Paris: Felix Alcan. 1935. Pp. 235. Price not stated.

THE excellence of Professor Leblanc's guidebook, as it may be termed, to the physiological anatomy of the nervous system resides in the simplicity of its arrangement and the clarity of its diagrams (not numbered, but scattered richly through the book). Synoptic tables provide additional reviews of the origin and endings of physiological systems from the periphery to the centre. The reader may look up any nerve-tract in cord or brain and find a precise and succinct summary of its constituents, its source, and its termination. The book fulfils its purpose admirably and can be recommended to anatomist and clinician alike.

A Textbook of Psychiatry. By D. K. Henderson, M.D., etc., Professor of Psychiatry, University of Edinburgh, and R. D. Gillespie, M.D., etc., Physician for Psychological Medicine, Guy's Hospital, London. Fourth edition. London: Humphrey Milford, Oxford University Press. 1936. Pp. 606. Price 18s. net.

FOUR years have elapsed since the third edition of this popular textbook appeared and was given favourable review in the JOURNAL. The text of the present issue has been revised and improved. In its class the book can once more be cordially praised as providing student and practitioner with a sound corpus doctrinæ in psychiatry by two writers of experience and ability. The fact that a fourth edition has been reached since the first publication in 1927 shows how highly the usefulness of the work has been regarded by those for whom it is intended.

Endocrine Tumours and other Essays. By Dr. F. Parkes Weber. London: H. K. Lewis & Co. 1936. Pp. 207.

IN his little volume of collected papers from the immense number he has contributed to medical literature Dr. Parkes Weber deals with several topics of interest to the student of the nervous system. That on endocrine tumours is perhaps one of the most valuable for its exact mise-au-point of present knowledge, and it has a large number of bibliographical references by way of appendix. Others deal with paroxysmal salivation, hemiatrophy and hypertrophy, Buerger's disease (of which Dr. Parkes Weber gave a description antedating that of Buerger himself), and with certain aspects of dreams. Anyone glancing through these readable pages will find something instructive on nearly every one, and will once more appreciate the remarkable erudition and wide-ranging mental activity of their distinguished author.

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